As filed with the Securities and Exchange Commission on October 10, 2023

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

ORCHESTRA BIOMED HOLDINGS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**3841**	**92-2038755**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

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New Hope, Pennsylvania 18938
(212) 862-5797
(Address, including zip code, and telephone number, including area code, of registrant’s principal executive offices)

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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box: ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold or issued until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and does not constitute the solicitation of an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED OCTOBER 10, 2023

PRELIMINARY PROSPECTUS

ORCHESTRA BIOMED HOLDINGS, INC.

Up to 22,221,440 Shares of Common Stock
Up to 1,932,841 Shares of Common Stock Issuable Upon the Exercise of Warrants
Up to 750,000 Warrants

This prospectus relates to the issuance by us of up to an aggregate of 1,932,841 shares of common stock, $0.0001 par value per share (the "Common Stock"), of Orchestra BioMed Holdings, Inc., a Delaware corporation ("Orchestra" or the "Company"), which consists of:

(a) up to 750,000 shares of Common Stock issuable upon the exercise of 750,000 private placement warrants (the "HSAC2 Warrant Shares") issued in a private placement to the sponsor (the "Sponsor") of Health Sciences Acquisitions Corporation 2 (the "HSAC2 Warrants") in connection with the initial public offering of Health Sciences Acquisitions Corporation 2 ("HSAC2");

(b) up to 675,000 shares of Common Stock issuable upon the exercise of 675,000 warrants (the "Officer and Director Warrant Shares") that were issued to certain officers and directors of the Company (the "Officer and Director Warrants") in connection with the forfeiture of 750,000 HSAC2 Warrants by the Sponsor as part of the Business Combination (75,000 of the initial 750,000 Officer and Director Warrants were forfeited in connection with the departure of Orchestra's former Chief Financial Officer); and

(c) up to 507,841 shares of Common Stock issuable upon the exercise of 507,841 private warrants (the "Orchestra Warrant Shares" and, together with the HSAC2 Warrant Shares and the Officer and Director Warrant Shares, the "Warrant Shares") issued in connection with the Business Combination (as defined below) in exchange for warrants issued by Orchestra BioMed, Inc., the Company's predecessor and now a wholly owned subsidiary of the Company (the "Orchestra Warrants" and, together with the HSAC2 Warrants and the Officer and Director Warrants, the "Warrants").

This prospectus also relates to the offer and sale from time to time, upon the expiration of lock-up agreements, if applicable, by:

(a) the selling stockholders named in this prospectus (including their permitted transferees, donees, pledgees and other successors-in-interest) (collectively, the "Selling Stockholders") of up to an aggregate of 22,221,440 shares (the "Resale Shares") of Common Stock, consisting of :

 (i) up to 10,675,809 shares of Common Stock issued to certain selling stockholders (the "Orchestra Affiliate Shares") on January 26, 2023 in connection with the Business Combination (as defined below);

 (ii) up to 10,070,645 shares of Common Stock held by the Sponsor and its affiliates (the "Sponsor Shares");

 (iii) up to 22,279 shares of Common Stock issued to certain selling stockholders in May 2023 in connection with the exercise of Company warrants;

 (iv) up to 750,000 HSAC2 Warrant Shares;

 (v) up to 675,000 Officer and Director Warrant Shares; and

 (vi) up to 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company;

(b) the selling warrantholder named in this prospectus (including its permitted transferees, donees, pledgees and other successors-in-interest) (the “Selling Warrantholder” and, together with the Selling Stockholders, the “Selling Securityholders”) of up to 750,000 HSAC2 Warrants.

On January 26, 2023, we consummated the previously announced business combination contemplated by the Agreement and Plan of Merger, dated as of July 4, 2022 (as amended by Amendment No. 1 to Agreement and Plan of Merger, dated July 21, 2022, and Amendment No. 2 to Agreement and Plan of Merger, dated November 21, 2022, the “Merger Agreement”), by and among HSAC2, a special purpose acquisition company incorporated as a Cayman Islands exempted company in 2020 (“HSAC2”), HSAC Olympus Merger Sub, Inc., a Delaware corporation and wholly owned subsidiary of HSAC2 (“Merger Sub”), and Orchestra BioMed, Inc. (“Legacy Orchestra”).

Our registration of the Resale Shares and the HSAC2 Warrants covered by this prospectus does not mean that the Selling Securityholders will offer or sell any of the Resale Shares or the HSAC2 Warrants. The Selling Securityholders may sell the Resale Shares and the HSAC2 Warrants covered by this prospectus in a number of different ways and at varying prices. For additional information on the possible methods of sale that may be used by the Selling Securityholders, you should refer to the section of this prospectus titled “*Plan of Distribution*” beginning on page 185 of this prospectus. We will receive the proceeds from any exercise of the Warrants for cash, but will not receive any of the proceeds from the resale of the Resale Shares or the HSAC2 Warrants sold by the Selling Securityholders, nor will we receive any proceeds as a result of the cashless exercise of Warrants, to the extent permitted.

No underwriter or other person has been engaged to facilitate the sale of the shares of our Common Stock or the Warrants in these offerings. The Selling Securityholders may be deemed to be “underwriters” within the meaning of the Securities Act of 1933, as amended (the “Securities Act”) of the Resale Shares and the HSAC2 Warrants that they are offering pursuant to this prospectus. We will bear all costs, expenses and fees in connection with the registration of the shares of our Common Stock and HSAC2 Warrants hereunder. The Selling Securityholders will bear all commissions and discounts, if any, attributable to their respective sales of the Resale Shares and the HSAC2 Warrants.

Our Common Stock is listed on the Nasdaq Global Market under the symbol “OBIO.” On October 6, 2023, the last reported sales price per share of our Common Stock was $7.09.

We are an “emerging growth company” and a “smaller reporting company” under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings with the Securities and Exchange Commission (the “SEC”).

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read this prospectus, together with additional information described under the heading “*Where You Can Find More Information*,” and any amendments or supplements carefully before you invest in any of our securities.

INVESTING IN OUR COMMON STOCK INVOLVES SUBSTANTIAL RISKS. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES DESCRIBED UNDER THE HEADING “RISK FACTORS” BEGINNING ON PAGE 7 OF THIS PROSPECTUS.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2023

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You should rely only on the information we have provided in this prospectus, any applicable prospectus supplement and any related free writing prospectus. Neither we nor the Selling Securityholders have authorized anyone to provide you with information different from that contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document, regardless of the time of delivery of this prospectus or any sale of a security. Since the date of this prospectus and any supplement to this prospectus, our business, financial condition, results of operations and prospects may have changed.

For Investors Outside the United States: The Selling Securityholders are offering to sell, and seeking offers to buy, the securities offered by this prospectus only in jurisdictions where offers and sales are permitted. Neither we nor the Selling Securityholders have done anything that would permit this offering or the possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities offered by this prospectus and the distribution of this prospectus outside the United States.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-1 that we filed with the SEC using the “shelf” registration process. Under this shelf registration process, the Selling Securityholders may, from time to time, sell the securities offered by them described in this prospectus. We will not receive any proceeds from the sale by such Selling Securityholders of the securities offered by them described in this prospectus. This prospectus also relates to the issuance by us of the shares of Common Stock issuable upon the exercise of the Warrants. We will not receive any proceeds from the sale of shares of Common Stock underlying the Warrants pursuant to this prospectus, except with respect to amounts received by us upon the exercise of the Warrants for cash.

Neither we nor the Selling Securityholders have authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus or any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. Neither we nor the Selling Securityholders take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the Selling Securityholders will make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.

We may also provide a supplement to this prospectus or a post-effective amendment to the registration statement to add information to, or update or change information contained in, this prospectus. You should read both this prospectus and any applicable prospectus supplement or post-effective amendment to the registration statement together with the additional information to which we refer you in the section of this prospectus entitled “*Where You Can Find More Information*.”

On January 26, 2023 (the “Closing Date”), the Company consummated the business combination contemplated by the Merger Agreement by and among HSAC2, Merger Sub and Legacy Orchestra. Pursuant to the Merger Agreement, (i) HSAC2 deregistered in the Cayman Islands in accordance with the Companies Act (2022 Revision) (As Revised) of the Cayman Islands and domesticated as a Delaware corporation in accordance with Section 388 of the Delaware General Corporation Law (the “Domestication”) and (ii) Merger Sub merged with and into Legacy Orchestra, with Legacy Orchestra as the surviving company in the merger and, after giving effect to such merger, continuing as a wholly owned subsidiary of Orchestra (the “Merger” and, together with the Domestication and the other transactions contemplated by the Merger Agreement, the “Business Combination”). As part of the Domestication, the Company’s name was changed from “Health Sciences Acquisitions Corporation 2” to “Orchestra BioMed Holdings, Inc.”

Unless the context indicates otherwise, references in this prospectus to the “Company,” “Orchestra,” “we,” “us,” “our” and similar terms refer to Orchestra BioMed Holdings, Inc., a Delaware corporation formerly known as Health Sciences Acquisitions Corporation 2, and its consolidated subsidiaries. “Legacy Orchestra” refers to Orchestra BioMed, Inc., the private Delaware corporation that is now our wholly owned subsidiary. References to “HSAC2” refer to Health Sciences Acquisitions Corporation 2, our predecessor company prior to the consummation of the Business Combination.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under “*Where You Can Find More Information*.”

References to information included on websites, or accessible through, websites do not constitute incorporation by reference of the information contained at or available through such websites, and you should not consider such information to be part of this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this report, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of clinical trials, research and development costs, regulatory approvals, timing, and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important factors that are in some cases beyond our control and may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this report include, but are not limited to, statements about:

- our ability to raise financing in the future;
- our ability to realize the anticipated benefits of the Business Combination;
- our success in retaining or recruiting, or changes required in, our officers, key employees or directors;
- our ability and/or the ability of third-party vendors and partners to manufacture our product candidates;
- our ability to source critical components or materials for the manufacture of our product candidates;
- our ability to achieve and sustain profitability;
- our ability to achieve our projected development and commercialization goals;
- the rate of progress, costs and results of our clinical studies and research and development activities;
- market acceptance of our product candidates, if approved;
- our ability to compete successfully with larger companies in a highly competitive industry;
- changes in our operating results, which make future operations results difficult to predict;
- serious adverse events, undesirable side effects that could halt the clinical development, regulatory approval or certification, of our product candidates;
- our ability to manage growth or control costs related to growth;
- economic conditions that may adversely affect our business, financial condition and stock price;
- our reliance on third parties to drive successful marketing and sale of our initial product candidates;
- our reliance on third parties to manufacture and provide important materials and components for our products and product candidates;
- our and our competitor's abilities to obtain necessary regulatory approvals and certifications for our product candidates in an uncomplicated and inexpensive manner;

- our ability to maintain compliance with regulatory and post-marketing requirements;
- adverse medical events, failure or malfunctions in connection with our product candidates and possible subjection to regulatory sanctions;
- healthcare costs containment pressures and legislative or administrative reforms, which affect coverage and reimbursement practices of third-party payors;
- our ability to protect or enforce our intellectual property, unpatented trade secrets, know-how and other proprietary technology;
- our ability to obtain necessary intellectual property rights from third parties;
- our ability to protect our trademarks, trade names and build our names recognition;
- our ability to maintain the listing of our Common Stock on The Nasdaq Stock Market LLC (“Nasdaq”);
- the success of our licensing agreements; and
- our public securities’ potential liquidity and trading.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations, and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this report and are subject to a number of risks, uncertainties, and assumptions described under the heading “Risk Factors” starting on page 7 of this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We do not plan to publicly update or revise any forward-looking statements contained herein whether as a result of any new information, future events, or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

SUMMARY OF THE PROSPECTUS

This summary highlights selected information included in this prospectus and does not contain all of the information that may be important to you in making an investment decision. This summary is qualified in its entirety by the more detailed information included in this prospectus. Before making your investment decision with respect to our securities, you should carefully read this entire prospectus, including the information under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations of Orchestra" and the financial statements included elsewhere in this prospectus.

The Company

We are a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. Our partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products we develop. We are led by a highly accomplished, multidisciplinary management team and a board of directors with extensive experience in all phases of therapeutic device development. Our business was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by our founding team. Our flagship product candidates are BackBeat Cardiac Neuromodulation Therapy ("BackBeat CNT") for the treatment of hypertension ("HTN"), the leading risk factor for death worldwide, and Virtue Sirolimus AngioInfusion Balloon ("Virtue SAB") for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. We have a strategic collaboration with Medtronic Plc ("Medtronic") for the development and commercialization of BackBeat CNT for the treatment of hypertension in patients indicated for a pacemaker. We have a strategic collaboration with Terumo Corporation and its U.S. subsidiary Terumo Medical Corporation (collectively, "Terumo") for the development and commercialization of Virtue SAB for the treatment of coronary and peripheral artery disease.

Pursuant to the Merger Agreement and the Business Combination, HSAC2 completed the Domestication and Merger Sub merged with and into Legacy Orchestra, with Legacy Orchestra as the surviving company in the Merger and, after giving effect to the Merger, continuing as a wholly owned subsidiary of HSAC2. In addition, as part of the Domestication, the Company's name was changed from "Health Sciences Acquisitions Corporation 2" to "Orchestra BioMed Holdings, Inc."

Our Common Stock is currently listed on the Nasdaq Global Market under the symbol "OBIO."

The mailing address of our principal executive office is 150 Union Square Drive, New Hope, PA 18938. Our telephone number is (215) 862-5797. For additional information about us, please see the sections of this prospectus titled "*Business*" and "*Management's Discussion and Analysis of Financial Condition and Results of Operations*."

See the section titled "*Risk Factors*" in this prospectus for a discussion of some of the risks related to the execution of our business strategy.

Recent Developments

On September 19, 2023, we announced that the U.S. Food and Drug Administration (the "FDA") granted us IDE approval to initiate our planned **B**radyc**A**rdia pa**C**ema**K**er with atrioventricular interval modulation for **B**lood pr**E**ssure tre**A**tmen**T** pivotal study (the "BACKBEAT pivotal study") of BackBeat CNT, also known as Atrioventricular Interval Modulation ("AVIM") therapy, to treat hypertension in patients indicated for a pacemaker. We currently expect to initiate enrollment of the BACKBEAT pivotal study before the end of 2023 following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals.

On August 8, 2023, we announced that the FDA granted us investigational device exemption approval with conditions to initiate our planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary in-stent restenosis ("ISR"). The conditional approval permits us to initiate enrollment of the Virtue ISR-US pivotal study following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals. We are also required to submit additional information to the FDA.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to our current agreement that could serve to restructure milestone payments as well as make other potential material modifications to that agreement. Until we gain

clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development, and commercialization plans for Virtue SAB may continue to be adversely impacted.

On October 6, 2023, the Company terminated and repaid the 2022 Loan and Security Agreement (as defined below). In connection with the repayment and termination, the Company repaid $10 million of principal and issued warrants to purchase 27,707 shares of Company Common Stock at an exercise price of $7.67 per share in lieu of a cash payment of approximately $212,500 due with respect to certain fees under the 2022 Loan and Security Agreement. The Company also paid approximately $849,000 of net interest, prepayment fees, and legal fees.

Emerging Growth Company and Smaller Reporting Company Status

We are an "emerging growth company," as defined in Section 2(a) of the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). As such, we are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Further, Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a Securities Act registration statement declared effective or do not have a class of securities registered under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that an emerging growth company can elect to opt out of the extended transition period and comply with the requirements that apply to non-emerging growth companies but any such election to opt out is irrevocable. We have elected not to opt out of such extended transition period which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of our financial statements with another public company which is neither an emerging growth company nor an emerging growth company which has opted out of using the extended transition period difficult or impossible because of the potential differences in accounting standards used.

We will remain an emerging growth company until the earliest of (1) the last day of the fiscal year following the fifth anniversary of the closing of the initial public offering of HSAC2 (or December 31, 2026), (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our Common Stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year, or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) the market value of our voting and non-voting Common Stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or (ii)(a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting Common Stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

Summary of Risk Factors

Risks Related to Our Business and Products

- We have a history of net losses, and we expect to continue to incur losses for the foreseeable future. If we ever achieve profitability, we may not be able to sustain it.

- If we do not achieve our projected development and commercialization goals, our business may be harmed.

- The clinical study process required to obtain regulatory approvals or certifications carries substantial risks and is lengthy and expensive with uncertain outcomes. If our clinical studies are unsuccessful or significantly delayed, or if we do not complete our clinical studies, our business may be harmed.

- Even if we obtain all necessary FDA approvals, our product candidates may not achieve or maintain market acceptance and may be subject to additional regulatory requirements post-approval.

- We may be unable to compete successfully with larger companies in our highly competitive industry.

- Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

- The sizes of the markets for product candidates have not been established with precision and may be smaller than we estimate.

- The long-term macroeconomic effects of the COVID-19 pandemic and any future pandemic or epidemic could adversely impact our business, including our clinical studies and financial condition.

- Our product candidates have in the past and may in the future be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval or certification, limit their commercial potential or result in significant negative consequences.

- If we do not manage our growth or control costs related to growth, our results of operations will suffer.

- Our information technology systems, or those of any of our contract research organizations (“CROs”), manufacturers, other contractors, consultants, collaborators or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Risks Related to Our Reliance on Third Parties

- We are, and expect to continue to be, highly dependent on partners to drive the successful marketing and sale of our initial product candidates. There is no assurance that we will be able to form and properly manage partnerships. There is no assurance that partnerships will be successful.

- We expect to be highly dependent on partners and third-party vendors to manufacture and provide important materials and components for our products and product candidates. There is no assurance that we will be able to properly manage our supply chain. Further, we currently do not have redundancy built into our supply chain.

- The failure of our manufacturing partners and component suppliers to meet regulatory quality standards applicable to their manufacturing processes could have an adverse effect on our business, financial condition and results of operations.

- We have limited pharmaceutical manufacturing experience and our contract manufacturing organizations ("CMOs") may experience development or manufacturing problems or delays in producing our products and planned or future products that could limit or prevent the potential growth of our revenue or increase our losses.

Risks Related to Government Regulation and Our Industry

- Regulatory compliance is expensive, complex and uncertain, and approvals or certifications can often be denied or significantly delayed. We may not obtain the necessary approvals or certifications and failure to obtain timely regulatory approval or certification, if at all, would adversely affect our business.

- Even if we obtain regulatory approval or certification for a product candidate, our products will remain subject to regulatory scrutiny and post-marketing requirements. Failure to comply with post-marketing regulatory requirements could subject us to enforcement actions, including substantial penalties, and might require us to recall or withdraw a product from the market.

- Our medical device products, if approved or certified, may cause or contribute to adverse medical events or be subject to failures or malfunctions that we are required to report to the FDA or similar foreign regulatory authorities, and if we fail to do so, we would be subject to sanctions that could harm our reputation, business, financial condition and results of operations. The discovery of serious safety issues with our products, or a recall of our products either voluntarily or at the direction of the FDA or another governmental authority, could have a negative impact on us.

- Virtue SAB is a drug/device combination, which may result in additional regulatory and other risks.

- If the FDA does not conclude that SirolimusEFR (as defined below) as a standalone product candidate satisfies the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for SirolimusEFR under Section 505(b)(2) are not as we expect, the approval pathway for SirolimusEFR may take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

- Healthcare cost-containment pressures and legislative or administrative reforms resulting in restrictive coverage and reimbursement practices of third-party payors could decrease the demand for our products, the prices that customers are willing to pay for those products and the number of procedures performed using our devices, which could have an adverse effect on our business.

Risks Related to Our Intellectual Property

- We may not effectively be able to protect or enforce our intellectual property, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

- We may be involved in litigation or other proceedings relating to patent, trade secret and other intellectual property rights, which could cause substantial costs and liability.

- If we cannot protect and control unpatented trade secrets, know-how and other proprietary technology, we may suffer competitive harm.

- Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

THE OFFERING

Issuer	Orchestra BioMed Holdings, Inc.
Issuance of Common Stock	
Shares of Common Stock offered by us	Up to 1,932,841 shares of Common Stock, issuable upon the exercise of (i)750,000 HSAC2 Warrants and (ii) 675,000 Officer and Director Warrants and (iii) 507,841 Orchestra Warrants.
Shares of Common Stock outstanding prior to exercise of all Warrants(1)	35,743,972 shares (as of October 6, 2023).
Shares of Common Stock outstanding assuming exercise of all Warrants(2)	37,704,520 shares (based on total shares outstanding as of October 6, 2023).
Use of Proceeds	We will receive up to an aggregate of approximately $21.2 million from the exercise of the Warrants, assuming the exercise in full of all of the Warrants for cash. We expect to use the net proceeds from the exercise of the Warrants for cash for working capital and general corporate purposes, which may include research and development expenditures, regulatory affairs expenditures, clinical trial expenditures, capital expenditures, acquisitions of new technologies and investments, business combinations and the repayment, refinancing, redemption or repurchase of indebtedness or capital stock. See "*Use of Proceeds*" elsewhere in this prospectus.
Resale of Common Stock and Warrants	
Shares of Common Stock offered by the Selling Securityholders	Up to 22,221,440 shares of Common Stock, consisting of (i) up to 10,675,809 Orchestra Affiliate Shares; (ii) up to 10,070,645 Sponsor Shares; (iii) up to 22,279 shares of Common Stock issued to certain selling stockholders in May 2023 in connection with the exercise of warrants; (iv) up to 750,000 HSAC2 Warrant Shares; (v) up to 675,000 Officer and Director Warrant Shares; and (vi) up to 22,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company.
Warrants offered by the Selling Warrantholder	Up to 750,000 HSAC2 Warrants, consisting of the HSAC2 Warrants not forfeited by the Sponsor as part of the Business Combination.
Use of Proceeds	We will not receive any proceeds from the sale of shares of Common Stock or Warrants by the Selling Securityholders, except with respect to amounts received by us upon the exercise of the Warrants for cash.
Lock-Up Restrictions	Certain of our stockholders are subject to certain restrictions on transfer until the termination of applicable lock-up periods. See "*Relationships and Related Party Transactions*" for further discussion.
Market for Common Stock	Our Common Stock is currently traded on the Nasdaq Global Market under the symbol "OBIO".
Risk Factors	See "*Risk Factors*" beginning on page 7 and other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in the securities being offered by this prospectus.

(1) The number of shares of Common Stock outstanding is based on an aggregate of 35,743,972 shares outstanding as of October 6, 2023, and excludes:

(a) 3,801,892 shares of Common Stock issuable upon the exercise of stock options outstanding under the Orchestra BioMed, Inc. 2018 Stock Incentive Plan (the "2018 Plan") at a weighted average exercise price of $7.96 per share;

(b) 777,425 shares of Common Stock issuable upon the exercise of stock options outstanding under the Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (the "2023 Plan") at a weighted average exercise price of $7.48 per share;

(c) 1,695,222 shares of Common Stock issuable upon the vesting of restricted stock units outstanding under the 2023 Plan;

(d) up to 1,064,050 shares of Common Stock available for future issuance under the 2023 Plan (which number does not include a possible annual increase on January 1 of each year beginning on January 1, 2024 and ending on (and including) January 1, 2032, in an amount equal to the lesser of (i) 4.8% of the total number of shares of Common Stock outstanding on December 31 of the immediately preceding year, (ii) 3,036,722 shares of Common Stock, and (iii) such number of shares of Common Stock determined by the board of directors of the Company (our "Board") or the compensation committee of our Board prior to January 1st of a given year);

(e) approximately 4,000,000 shares of Common Stock to be issued if the Final Milestone Event (as defined below) is achieved.

(f) 750,000 shares of Common Stock issuable upon the exercise of the HSAC2 Warrants, with an exercise price of $11.50 per share;

(g) 675,000 shares of Common Stock issuable upon the exercise of the Officer and Director Warrants, with an exercise price of $11.50 per share; and

(h) 507,841 shares of Common Stock issuable upon the exercise of the Orchestra Warrants, with a weighted average exercise price of $9.01 per share; and

(i) up to 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company.

(2) The number of shares of Common Stock outstanding is based on an aggregate of 35,743,972 shares outstanding as of October 6, 2023, and excludes (a) through (e) in footnote (1) above.

RISK FACTORS

Investing in our securities involves risks. Before you make a decision to buy our securities, in addition to the risks and uncertainties discussed above under "Special Note Regarding Forward-Looking Statements," you should carefully consider the specific risks set forth herein. If any of these risks actually occur, it may materially harm our business, financial condition, liquidity and results of operations. As a result, the market price of our securities could decline, and you could lose all or part of your investment. Additionally, the risks and uncertainties described in this prospectus are not the only risks and uncertainties that we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may become material and adversely affect our business.

Risks Related to Our Business and Products

We have a history of net losses, and we expect to continue to incur losses for the foreseeable future. If we ever achieve profitability, we may not be able to sustain it

We have incurred losses since our inception and expect to continue to incur losses for the foreseeable future. We have reported a net loss of approximately $23.0 million for the six months ended June 30, 2023 and net losses of approximately $33.6 million and $23.0 million for the years ended December 31, 2022 and 2021, respectively. As a result of these losses, as of June 30, 2023, we had an accumulated deficit of approximately $222.7 million. We expect to continue to incur net losses for the foreseeable future.

We will continue to incur substantial expenses without corresponding revenues unless and until we are able to obtain regulatory approval or certification and successfully commercialize some of our product candidates. To date, we have generated only limited revenue from our products, and we expect to incur significant expenses to complete our clinical program for our product candidates in the United States and elsewhere. We may never be able to obtain regulatory approval or certification for the marketing of our product candidates in the United States or internationally. Even if we are able to commercialize some of our products or product candidates, there can be no assurance that we will generate significant revenues or ever achieve profitability. We expect to continue to incur significant sales and marketing, research and development, regulatory and other expenses as we expand our marketing efforts to increase adoption of our products, expand existing relationships with our customers, obtain regulatory approvals or certifications for our product candidates, conduct clinical studies on our existing and planned product candidates and develop new product candidates or add new features to our existing products. In addition, we expect our selling, general and administrative expenses to increase due to the additional costs associated with being a public company. The net losses that we incur may fluctuate significantly from period to period. As a result of these increased expenditures, we will need to generate significant additional revenue in order to offset our operating expenses and achieve and sustain profitability. Accordingly, we may not achieve or maintain profitability, and we may continue to incur significant losses in the future. Even if we achieve profitability, we cannot be sure that we will remain profitable for any substantial period of time. If we do not achieve or sustain profitability, it will be more difficult for us to finance our business and accomplish our strategic objectives, either of which would have a material adverse effect on our business, financial condition, results of operations and prospects and may cause the market price of our Common Stock to decline.

We currently have a limited operating history and limited sources of revenue and may never become profitable

We commenced substantive operations in 2018. Our wholly-owned subsidiary Caliber Therapeutics, LLC ("Caliber") commenced operations in 2008, our wholly-owned subsidiary BackBeat Medical, LLC ("BackBeat") commenced operations in 2010 and our wholly-owned subsidiary FreeHold Surgical, LLC ("FreeHold") commenced operations in 2010. Our limited operating history makes it difficult to evaluate our current business and predict our future results, prospects or viability. To date, we have not generated significant revenue. Our ability to generate substantial revenue and ultimately become profitable depends primarily upon our ability, alone or with our partners, to successfully obtain regulatory approval and certification for and successfully commercialize our product candidates. Our ability to generate future revenue from our products or any existing or future product candidates also depends on a number of additional factors, including our or our partners' ability to:

- successfully complete clinical development of our product candidates, including necessary clinical studies;
- successfully develop the manufacturing processes for our product candidates;

- establish and maintain supply and manufacturing relationships with third parties that ensure adequate and legally-compliant production of our product candidates;
- complete and submit necessary applications for regulatory approvals and certifications for our product candidates in the United States and elsewhere;
- obtain and maintain requisite regulatory approvals and certifications for our product candidates in the United States and elsewhere;
- comply with regulations enforced by the FDA, and other comparable regulatory authorities with respect to our marketing of products and product candidates or modified products or product candidates;
- obtain necessary FDA or foreign regulatory approvals or certifications, for our product candidates or for future product modifications or indication expansions for any of our product candidates that receives regulatory approval or certification;
- obtain coverage and adequate reimbursement from third-party payors, including government and private payors, for our product candidates;
- find distribution partners to help us sell, market and distribute our products globally;
- achieve market acceptance for our products;
- establish, maintain and protect our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with drug/device and software/device combination product development, including that our product candidates may not advance through development or achieve the endpoints of applicable clinical studies, we are unable to predict the timing or amount of our expenses, or if or when we will achieve or maintain revenues or profitability. In addition, our expenses could increase beyond expectations if we decide to or are required by the FDA or foreign regulatory authorities or notified bodies to perform non-clinical tests or clinical studies or trials for our product candidates in addition to those that we currently anticipate. If we complete the development and regulatory processes of our product candidates, we or our partners anticipate incurring significant costs associated with launching and commercializing our product candidates. Even if we generate revenues from the sale of our products (or through the sale of products by our partners), we may not be profitable and may need to obtain additional funding to continue operations. If we fail to achieve profitability or do not sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

If we do not achieve our projected development and commercialization goals, our business may be harmed

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development and commercialization goals, which we sometimes refer to as milestones. These milestones include the commencement or completion of scientific studies and clinical studies and the submission of regulatory applications. We base these milestones on a variety of assumptions, which are subject to numerous risks and uncertainties. Further, our collaboration agreement with Terumo, as further described herein, includes payments tied to the achievement of certain milestones, which in some cases, must be achieved by a specified calendar date. Other future collaboration agreements may have similar provisions. There is a risk we will not achieve these milestones on a timely basis or at all. Even if we achieve these milestones, the actual timing of the achievement of these milestones can vary dramatically compared to our estimates, often for reasons beyond our control, depending on numerous factors, including:

- our ability and/or the ability of third-party vendors and partners to manufacture our product candidates;
- our ability to source critical components or materials for the manufacture of our product candidates;
- the rate of progress, costs and results of our clinical studies and research and development activities;

- our ability to identify and enroll patients who meet clinical study eligibility criteria;
- the extent of scheduling conflicts with participating physicians and clinical institutions;
- adverse reactions reported during clinical studies or commercialization;
- the ability of our product candidates to meet the standards for regulatory approval or certification;
- the receipt of marketing approvals, clearances or certifications by our competitors and by us from the FDA and other regulatory agencies or notified bodies; and
- other actions by regulators, including actions related to a class of products.

If we do not meet these milestones for our products or if we are delayed in achieving these milestones, the development and commercialization of new product candidates, modifications of existing products or sales of existing products for new indications may be prevented or delayed, which could damage our reputation or materially adversely affect our business. Further, we may not receive milestone-based payments from partners on a timely basis or at all, which may have an adverse impact on our anticipated financial resources. In addition, Terumo has the right to terminate, and other partners may have the right to terminate or renegotiate, agreements if certain milestones are not achieved at all or on a timely basis. Even if we achieve a milestone for a product or product candidate, market acceptance for the product or product candidate is not assured. See "*— Risks Related to Our Reliance on Third Parties — We did not meet the target achievement dates relating to certain milestone payments, and we may not meet other target achievement dates relating to additional milestone payments, under our manufacturing and distribution agreement with Terumo, which may have an adverse effect on our relationship with Terumo and our results of operations*."

The clinical study process required to obtain regulatory approvals or certifications carries substantial risks and is lengthy and expensive with uncertain outcomes. If our clinical studies are unsuccessful or significantly delayed, or if we do not complete our clinical studies, our business may be harmed

In order to obtain approval of a pre-market approval application (a "PMA") from the FDA for a device, such as our Virtue SAB drug/device combination product candidate, BackBeat CNT or CNT-HF which is designed to be integrated with the collaboration of device manufacturers into their existing medical devices such as pacemakers, as well as other future product candidates, or marketing approval for a new drug, such as our extended release formulation of sirolimus called "SirolimusEFR" a standalone product candidate, we must conduct well-controlled clinical studies designed to assess the safety and efficacy of the product candidate. Clinical development is a long, expensive and uncertain process and is subject to delays and to the risk that products may ultimately prove unsafe or ineffective in treating the indications for which they are designed. Completion of the clinical studies required to support a marketing authorization (inclusive of any application or approval for clinical use or commercial sale in a given market) usually takes several years or more. We cannot assure you that we will successfully complete clinical testing of our products within the periods we have planned, or at all. Even if we achieve positive interim or preliminary results in clinical studies, these results do not necessarily predict final results, and positive results in early trials do not necessarily indicate success in later trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies have suffered significant setbacks in advanced clinical studies, even after receiving positive results in earlier trials. Any of our products may malfunction or may produce undesirable adverse effects that could cause us or regulatory authorities to interrupt, delay or halt clinical studies. We, the FDA, or another regulatory authority may suspend or terminate clinical studies at any time to avoid exposing trial participants to unacceptable health risks.

Additionally, the FDA or other regulatory authorities or notified bodies may disagree with our interpretation of the data from our preclinical studies and clinical studies, or may find the clinical study design, conduct or results inadequate to prove safety or efficacy, and may require us to pursue additional preclinical studies or clinical studies, which could further delay or prevent the approval or certification of our products. The data we collect from our preclinical studies and clinical studies may not be sufficient to support potential FDA or foreign approval or certification, and if we are unable to demonstrate the safety and efficacy of our product candidates in our clinical studies, we will be unable to obtain regulatory approval or certification to market our products.

We have in the past and may in the future experience unforeseen events during, or because of, the clinical study process that could delay or prevent us from receiving regulatory approval or certification for new products, modification of existing products, or approval or certification of new indications for existing products including:

- we may be unable to generate sufficient preclinical toxicology or other in vivo or in vitro data to support the initiation or continuation of clinical studies;
- the FDA or similar foreign regulatory authorities may find the product candidates are not sufficiently safe for investigational use in humans;
- officials at the FDA or similar foreign regulatory authorities may interpret data from preclinical testing and clinical studies in less favorable ways than we do;
- there may be delays or failures in obtaining regulatory authorization from the FDA or other regulatory authorities to commence a clinical study;
- there may be delays or failures in the manufacture or supply of devices and/or drugs for use in clinical studies;
- there may be delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- there may be delays in identifying, recruiting and training suitable investigators;
- there may be delays in obtaining institutional review board (“IRB”) or ethics committee (“EC”) approvals or governmental approvals, authorizations or allowances to conduct clinical studies at prospective sites;
- enrollment in our clinical studies may be slower than we anticipate, or we may experience high drop-out rates of subjects from our clinical studies, resulting in significant delays;
- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical studies or failing to return for post-treatment follow-up;
- failure by our CROs, other third parties or us to adhere to clinical study protocols, failure to perform in accordance with the FDA’s or any other regulatory authority’s good clinical practice requirements (“GCPs”), or applicable regulatory guidelines in other countries, or occurrence of adverse events in trials of comparable products conducted by other companies;
- the occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- we may have to amend clinical study protocols or conduct additional studies to reflect changes in regulatory requirements or guidance, which we may be required to submit to an IRB or EC and/or regulatory authorities for re-examination;
- the cost of clinical studies may be greater than we anticipate;
- we may have trouble in managing multiple clinical sites;
- our clinical studies may produce negative or inconclusive results, or may not meet the level of statistical significance required by the FDA or other regulatory authorities, and we may decide, or regulators may require us, to conduct additional clinical or preclinical testing or to abandon programs;
- the FDA or similar foreign regulatory authorities may find our or our suppliers’ manufacturing processes or facilities unsatisfactory;

- the FDA or similar foreign regulatory authorities may change their approval policies or adopt new regulations that may negatively affect or delay our ability to bring a product candidate to market or receive approvals or certification to treat new indications;
- our regulatory approvals may be tied to our current supply chain, especially for combination products, and if we need to change locations or vendors, we may be required to repeat preclinical testing, including biocompatibility testing, that would delay or prevent our ability to produce clinical or commercial products;
- we may be required to transfer manufacturing processes to larger-scale facilities operated by a CMO, and could be adversely affected by delays or failures by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties may be unwilling or unable to satisfy their contractual obligations to us.

Patient enrollment in clinical studies and completion of patient follow-up depend on many factors, including the size of the patient population, the nature of the trial protocol, the proximity of patients to clinical sites, the eligibility criteria for the clinical study, patient compliance, competing clinical studies and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new treatments that may be approved for the indications we are investigating. In addition, patients participating in our clinical studies may drop out before completion of the trial or experience adverse medical events unrelated to our product candidates. Delays in patient enrollment or failure of patients to continue to participate in a clinical study may delay commencement or completion of the clinical study, cause an increase in the costs of the clinical study and delays, or result in the failure of the clinical study. In addition, disruptions caused by the COVID-19 pandemic, including any strains or variants of the virus, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical studies.

We could also encounter delays if a clinical study is suspended or terminated by us, by the IRBs of the institutions at which such studies are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols, inspection of the clinical study operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using the investigational product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical study. If we experience delays in the completion of, or termination of, any clinical study, the approval, certification and commercial prospects of our device will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical studies will increase our costs, slow down the approval or certification process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

Failures or perceived failures in our clinical studies will delay and may prevent our product candidate development and regulatory approval or certification process, damage our business prospects and negatively affect our reputation and competitive position

Failure can occur at any stage of clinical testing. Our clinical studies may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and non-clinical testing in addition to those we have planned. Our failure to adequately demonstrate the safety and efficacy of our system or any product we may develop in the future would prevent receipt of regulatory approval or certification and, ultimately, the commercialization of that product or indication for use. Further, regulators may determine that our financial relationships with certain principal investigators who provide us with consulting services from time to time for which we separately compensate them resulted in a perceived or actual conflict of interest that may have affected the interpretation of a study, the integrity of the data generated at the applicable clinical study site or the utility of the clinical study itself. Even if our future products are approved in the United States, commercialization of our product candidates in foreign countries would require approval by regulatory authorities or certification by notified bodies in those countries. Approval and certification procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical studies. Any of these occurrences could have an adverse effect on our business, financial condition and results of operations.

Clinical studies must be conducted in accordance with the laws and regulations of the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs at the medical institutions where the clinical studies are conducted. In addition, clinical studies must be conducted with supplies of our product candidates produced under current good manufacturing practice ("cGMP"), requirements and other regulations. Furthermore, we rely on CROs, consultants and clinical study sites to ensure the proper and timely conduct of our clinical studies and while we have agreements governing their committed activities, we have limited influence over their actual performance. We depend on our collaborators and on medical institutions and CROs to conduct our clinical studies in compliance with GCP requirements. To the extent our collaborators or the CROs fail to enroll participants for our clinical studies, fail to conduct the study to GCP standards or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both. In addition, clinical studies that are conducted in countries outside the United States may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements and the engagement of non-U.S. CROs, as well as expose us to risks associated with clinical investigators who are unknown to the FDA, and different standards of diagnosis, screening and medical care.

Even if we obtain all necessary FDA approvals, our product candidates may not achieve or maintain market acceptance and may be subject to additional regulatory requirements post-approval

Even if we obtain FDA approval of our product candidates, or new indications for our products, market acceptance of our products in the healthcare community, including physicians, patients and third-party payors, will depend on many factors, including:

- our ability to provide incremental clinical and economic data that shows the safety and clinical efficacy and cost-effectiveness of, and patient benefits from, our products;
- the availability of alternative treatments;
- whether our products are included on insurance company formularies or coverage plans;
- the willingness and ability of patients and the healthcare community to adopt new technologies;
- customer demand;
- liability risks generally associated with the use of new product candidates;
- the training required to use a new product candidate;
- perceived inadequacy of evidence supporting clinical benefits or cost-effectiveness over existing alternatives;
- the convenience and ease of use of our products relative to other treatment methods;
- the pricing and reimbursement of our products relative to other treatment methods; and
- the marketing and distribution support for our products.

Even if we obtain all necessary FDA approvals, our products may fail to achieve market acceptance. If our products achieve market acceptance, they may not maintain that market acceptance over time if competing products or technologies are introduced that are received more favorably or are more cost-effective. Failure to achieve or maintain market acceptance would limit our ability to generate revenue and would have a material adverse effect on our business, financial condition, results of operations and prospects. Further, our products are subject to ongoing regulatory oversight and may require additional clinical data to support maintenance of regulatory approvals.

We may be unable to compete successfully with larger companies in our highly competitive industry

The medical technology and pharmaceutical industries are highly competitive and the medical device industry is characterized by rapid and significant change. Many of our current and potential competitors have substantially greater financial, manufacturing, marketing, and technical resources than we do. Larger competitors may have substantially larger sales and marketing operations than we or our partners have or plan to have and may have greater name recognition. This may allow those competitors to spend more time with potential customers and to focus on a larger number of potential customers, which would give them a significant advantage over the sales and marketing team we would use and our international distributors in making sales.

Larger competitors may also have broader product lines, which enable them to offer customers bundled purchase contracts and quantity discounts. These competitors may have more experience than we have in research and development, marketing, manufacturing, preclinical testing, conducting clinical studies, obtaining FDA and foreign regulatory approvals or certifications and marketing approved or certified products. Our competitors may discover technologies and techniques, or enter into partnerships and collaborations, to develop competing products that are more effective or less costly than our products or the products we may develop. There can be no assurance that other companies will not succeed in developing or marketing devices and products that are more effective than our technology or products or that would render our technology or products obsolete or noncompetitive. Academic institutions, government agencies, and other public and private research organizations may seek patent protection regarding potentially competitive products or technologies and may establish exclusive collaborative or licensing relationships with our competitors. Our competitors may be better equipped than we are to respond to competitive pressures. Competition will likely intensify.

Additionally, many companies in the healthcare industry, including healthcare provider systems, are consolidating to create new companies with greater market power, and we expect that to continue. As the healthcare industry consolidates, competition to provide goods and services to industry participants will become more intense. These industry participants may try to use their market power to negotiate price concessions or reductions for medical devices including those produced by us. If we reduce our prices because of consolidation in the healthcare industry, our revenue would decrease and our consolidated earnings, financial condition, or cash flows would suffer.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the level of demand for our products and any approved or certified products, which may vary significantly;
- expenditures that we may incur to acquire, develop or commercialize additional products and technologies;
- the ability to obtain, and timing and cost of obtaining regulatory approvals or certifications for planned or future products or indications;
- the degree of competition in our industry and any change in the competitive landscape of our industry, including consolidation among our competitors or future partners;
- coverage and reimbursement policies with respect to our products, if approved or certified, and potential future products that compete with our products;
- the timing and success or failure of preclinical studies or clinical studies for our products or any future products we develop or competing products;
- the timing of customer orders or medical procedures using our products and the number of available selling days in any quarterly period, which can be impacted by holidays, the mix of products sold and the geographic mix of where products are sold;

- the timing and cost of, and level of investment in, research, development, regulatory approval or certification and commercialization activities relating to our products, which may change from time to time;
- the cost of manufacturing our products, which may vary depending on the quantity of production and the terms of our agreements with third-party suppliers and manufacturers; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, it could have a material adverse effect on our business, financial condition, results of operations or prospects.

The sizes of the markets for product candidates have not been established with precision, and may be smaller than we estimate

Our estimates of the annual total addressable markets for our product candidates are based on a number of internal and third-party estimates, including, without limitation, the number of patients with specified diseases and the assumed prices at which we will be able to sell any products we develop in various markets. While we believe our assumptions and the data underlying our estimates are reasonable, these assumptions and estimates may not be correct and the conditions supporting our assumptions or estimates may change at any time, thereby reducing the predictive accuracy of these underlying factors. In addition, our estimates of the sizes of the peripheral artery disease (“PAD”) and coronary artery disease (“CAD”) patient population may include patients who are asymptomatic or in the early stages of disease; these patients might never progress to more advanced disease stages and, accordingly, might never be likely candidates for treatment with our products. As a result, our estimates of the annual total addressable market for our current or future products may prove to be incorrect. If the actual number of patients who would benefit from our products, the price at which we will be able to sell future products, or the annual total addressable market for our products is smaller than we have estimated, it may impair future sales of any product we develop and have an adverse impact on our business.

The long-term macroeconomic effects of the COVID-19 pandemic and any future pandemic or epidemic could adversely impact our business, including our clinical studies and financial condition

Outbreaks of contagious disease, including COVID-19, or other adverse public health developments in the U.S. or worldwide could have a material adverse effect on our business, including our clinical trials and financial condition. While many of the direct impacts of the COVID-19 pandemic have eased, the longer-term macroeconomic effects on global supply chains, inflation, labor shortages and wage increases continue to impact many industries, including ours. Moreover, with the potential for new strains of existing viruses to emerge, or other pandemics or epidemics, governments and businesses may re-impose aggressive measures to help slow the spread of disease in the future.

Long-term macroeconomic effects from a pandemic or epidemic, including from supply and labor shortages and workforce reductions in response to challenging economic conditions, may have an adverse impact on our business. In addition, COVID-19 caused, and any future pandemic or epidemic may cause, delays with respect to regulatory approvals or certifications for clinical studies, the initiation of clinical studies and the coordination of follow-up with respect to clinical studies, as well as delays in receiving supplies and third-party testing results from vendors. The emergence of a new pandemic or epidemic may also cause us to experience additional disruptions that could severely impact our business and clinical studies, including:

- delays or difficulties in enrolling patients in our clinical studies;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;

- diversion of healthcare resources away from the conduct of clinical studies, including the diversion of hospitals serving as our clinical study sites and hospital staff supporting the conduct of our clinical trials;

- interruption of key clinical study activities, such as clinical study site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical study subject visits and study procedures, the occurrence of which could affect the integrity of clinical study data;

- risk that participants enrolled in our clinical studies will contract the contagious disease while the clinical study is ongoing, which could impact the results of the clinical study, including by increasing the number of observed adverse events;

- limitations in employee resources that would otherwise be focused on the conduct of our clinical studies, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;

- delays in receiving authorizations, allowances or approvals from local regulatory authorities to initiate our planned clinical studies;

- delays in clinical sites receiving the supplies and materials needed to conduct our clinical studies, including interruption in global shipping that may affect the transport of clinical study materials, such as investigational materials used in our clinical studies;

- changes in local regulations as part of a response to such pandemic or epidemic which may require us to change the ways in which our clinical studies are conducted, which may result in unexpected costs, or the discontinuation of such clinical studies altogether;

- interruptions or delays in preclinical studies due to restricted or limited operations at research and development laboratory facilities;

- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and

- refusal of the FDA to accept data from clinical studies in affected geographies.

The full extent of the impact and effects of COVID-19, and any future pandemics or epidemics, will depend on future developments, including, among other factors, how rapidly variants develop, availability, acceptance and effectiveness of vaccines along with related travel advisories, quarantines and restrictions, the recovery time of the disrupted supply chains and industries, the impact of labor market interruptions, the impact of government interventions, and uncertainty with respect to the duration of the global economic slowdown. COVID-19, or any future pandemics or epidemics, and resulting impacts on the financial, economic and capital markets environment, and future developments in these and other areas present uncertainty and risk with respect to our business and financial results.

Interim, "top-line" and preliminary data from our clinical studies that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical studies. Interim data from clinical studies that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical studies continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our Common Stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical study is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval or certification for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Our product candidates have in the past and may in the future be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval or certification, limit their commercial potential or result in significant negative consequences

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval or certification by the FDA or other comparable foreign regulatory authorities or notified bodies.

During the conduct of clinical studies, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical studies, or as use of these product candidates becomes more widespread if they receive regulatory approval or certification, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical studies or, in some cases, after they are made available to patients on a commercial scale following approval or certification.

For example, during the initial study period for MODERATO I, there were eleven serious adverse events (“SAEs”) in seven of the 27 study patients. One event was adjudicated as probably related to the implant procedure for the Moderato device. Four events in four patients were adjudicated as possibly related to the Moderato device (atrial fibrillation, myocardial infarction with symptoms of heart failure, cardiac asthma, and arrhythmia due to ventricular oversensing).

During the extended 21-month follow-up period, that included 24 patients who continued with BackBeat CNT, there were 25 SAEs in twelve patients. Five events in three patients were adjudicated as possibly device related. These included two events of atrial fibrillation in the same patient, pneumonia with cardiac decompensation and dyspnea with cardiac decompensation in one patient, and cardiac decompensation in one patient.

For the MODERATO II study, there were no major adverse cardiac events (“MACE”) in the BackBeat CNT group and three MACE in two patients in the control group (one death from cancer and two cardiac events) at six months. During the randomized phase of the study, there were eight SAEs in four patients in the control group (n=21) and none in the treatment group (n=26). During the extended 18-month follow-up period that included treatment patients (n=26) and crossover-to-treatment patients (n=14), there were 26 SAEs in 16 patients. Over the entire three-year period of the SABRE study, a total of 66 SAEs occurred in 32 of the 50 study patients.

If any serious adverse events occur, clinical studies or commercial distribution of any product candidates or products we develop could be suspended or terminated, and our business could be seriously harmed. Treatment-related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us to cease further development of, deny approval of, or require us to cease selling any product candidates or products for any or all targeted indications. If we are required to delay, suspend or terminate any clinical study or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated. Additionally, if one or more of our product candidates receives marketing approval or certification and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may suspend, limit or withdraw approvals or certifications of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical studies or post-approval studies;
- we may be required to create a risk evaluation and mitigation strategy (“REMS”) or similar risk management measures, which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved or certified, and could seriously harm our business.

We depend on attracting, retaining and developing key management, clinical, scientific, regulatory, quality, marketing and other expert personnel, and losing these personnel could impair the development and sales of our products or product candidates

We are highly dependent on our senior management and other key personnel. Our success depends on our continued ability to attract, retain, develop and motivate highly qualified management, clinical, scientific and sales and marketing personnel. Although we have entered into employment agreements with certain of our executive officers, our employees, including our executive officers, are employed “at will,” and each employee can terminate his or her employment with us at any time. We also do not maintain “key person” insurance policies on any of our officers or our other employees. The competition for qualified personnel in the medical innovation industry is intense, and we may incur significant costs to attract and retain them. We will need to hire additional personnel as we continue to expand our development activities and drive sales of our products or product candidates. We may not attract, retain and develop quality personnel on acceptable terms due to the competition for such personnel. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

If we make acquisitions, we could incur significant costs and encounter difficulties that harm our business

In the ordinary course of our business, we expect to from time to time evaluate the acquisition of, investment in or in-license of complementary products, technologies or businesses, although we do not currently have any agreements, arrangements or commitments with respect to any potential acquisition, investment or license. If we engage in such acquisitions, investments or in-licenses, we may incur significant transaction and integration costs and have difficulty integrating the acquired personnel, operations, products or technologies or otherwise realizing synergies or other benefits from the acquisitions, investments or in-licenses. The

integration process could result in the loss of key employees, loss of key customers, loss of key vendors, decreases in revenue and increases in operating costs, as well as the disruption of our business. Acquisitions may disrupt our ongoing business, divert the time of our management and employees, increase our expenses, subject us to liabilities and increase our risk of litigation, all of which could harm our business. If we use cash to acquire companies, products or technologies, it may divert resources otherwise available for other purposes or increase our debt. If we use our capital stock to acquire companies, products or technologies, we may experience a change of control or our stockholders may experience substantial dilution or both. In addition, anticipated benefits of any future acquisitions may not materialize. Any of these risks, if realized, could materially and adversely affect our business, financial condition, results of operation and prospects.

If we do not manage our growth or control costs related to growth, our results of operations will suffer

We intend to grow our business by commercializing our product candidates with partners when approved and, expanding our product development pipeline, possibly through acquisitions or other business combinations. Growth could place significant strain on our management, employees, operations, operating and financial systems, and other resources. To accommodate significant growth, we could be required to open additional facilities, expand and improve our information systems and procedures and hire, train, motivate and manage a growing workforce, all of which would increase our costs. Our systems, facilities, procedures and personnel may not be adequate to support our future operations. Further, we may not maintain or accelerate our current growth, manage our expanding operations or achieve planned growth on a timely and profitable basis.

Litigation and other legal proceedings may adversely affect our business

From time to time we may be involved in various litigation matters, which could have an adverse impact on our reputation, business and financial condition and divert the attention of our management from the operation of our business. Claims arising out of actual or alleged violations of the law could be asserted against us by individuals, either individually or through class actions, by governmental entities in civil or criminal investigations and proceedings by other entities. These claims could be asserted under a variety of laws, including but not limited to patent, trade secret and other intellectual property matters, product liability claims, employee claims, tort or contract claims, and federal regulatory investigations. These actions could expose us to adverse publicity and to substantial monetary damages and legal defense costs, injunctive relief and criminal and civil fines and penalties.

Product liability and other claims against us may reduce demand for our products or result in substantial damages

Our business exposes us to potential liability for risks that may arise from the clinical testing of our product candidates, the use of our products by physicians, and the manufacture and sale of any approved products. Individuals may bring a product liability claims against us, including frivolous lawsuits, if one of our products causes, or merely appears to have caused, an injury.

We currently have product liability insurance for $6.0 million per occurrence with an annual aggregate maximum of $6.0 million.

We cannot assure, however, that product liability claims will not exceed our insurance coverage limits or that such insurance coverage limits will continue to be available on acceptable terms, or at all. Our insurers may also claim that certain claims are not within the scope of our product liability insurance. A product liability claim, recall, or other claim regarding uninsured liabilities or for amounts over insured liabilities could have a material adverse effect on our business, financial condition, results of operations and prospects. Any product liability claim or series of claims or class actions brought against us, with or without merit, could result in:

- liabilities that substantially exceed our insurance levels, which we would then be required to pay from other sources, if available;

- an increase in our product liability insurance rates or the inability to renew or obtain product liability insurance coverage in the future on acceptable terms, or at all;

- withdrawal of clinical study volunteers or subjects;

- damage to our reputation and the reputation of our product candidates;

- regulatory investigations that could require costly recalls or product modifications;
- litigation costs; and
- diversion of our management's attention from managing our business.

The misuse or off-label use of our products may harm our reputation in the marketplace, result in injuries that lead to product liability suits or result in costly investigations, fines or sanctions by regulatory bodies if we are deemed to have engaged in the promotion of these uses, any of which could be costly to our business

Any products that we market will be subject to the limitations on indicated uses as specified in their respective approvals or certifications. Uses outside of the approved or certified indications for use are known as "off-label uses." We cannot prevent a physician from using our products off-label, when, in the physician's independent professional medical judgment, he or she deems it appropriate. There may be increased risk of injury to patients if physicians attempt to use our products off-label. Furthermore, the use of our products for indications, other than those approved or certified by the FDA or by any foreign regulatory authority or notified body, may not effectively treat such conditions, which could harm our reputation in the marketplace among physicians and patients.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved or certified. In particular, a product may not be promoted for off-label uses. If the FDA or any foreign regulatory body determines that our promotional materials or training constitute promotion of an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance or imposition of an untitled letter, which is used for violators that do not necessitate a warning letter, injunction, seizure, civil fine or criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action under other regulatory authority, such as false claims laws, if they consider our business activities to constitute promotion of an off-label use, which could result in significant penalties, including, but not limited to, criminal, civil and administrative penalties, damages, fines, disgorgement, exclusion from participation in government healthcare programs and the curtailment of our operations.

In addition, physicians may misuse our products, or use improper techniques if they are not adequately trained, potentially leading to injury and an increased risk of product liability. If so, we may become subject to costly litigation by our customers or their patients. Product liability claims could divert management's attention from our core business, be expensive to defend and result in sizable damage awards against us that may not be covered by insurance.

Our information technology systems, or those of any of our CROs, manufacturers, other contractors, consultants, collaborators or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations

Despite the implementation of security measures, our information technology systems and those of our current and any future CROs and other contractors, consultants, collaborators and third-party service providers, are vulnerable to attack and damage from computer viruses and malware (e.g., ransomware), malicious code, hacking, cyberattacks, phishing attacks and other social engineering schemes, cybersecurity threats, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failure, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are, from time to time, subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of, or access to, personally identifiable information or individually identifiable health information, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors or organizations with which we have formed strategic relationships. Notifications and follow-up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical study data from completed or future clinical studies could result in delays in our regulatory approval or certification efforts and significantly increase our costs to recover or reproduce the lost data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

We must successfully maintain and upgrade our information technology systems, and our failure to do so could have a material adverse effect on our business, financial condition and results of operations

As we expand, in order to remain competitive, we will need to significantly expand and improve our information technology systems and personnel to support historical and expected future growth. As such, we will continue to invest in and implement, significant modifications and upgrades to our information technology systems and procedures, including replacing legacy systems with successor systems, making changes to legacy systems or acquiring new systems with new functionality, hiring employees with information technology expertise and building new policies, procedures, training programs and monitoring tools. These types of activities subject us to inherent costs and risks associated with replacing and changing these systems, fulfill customer orders, potential disruption of our internal control structure, substantial capital expenditures, additional administration and operating expenses, acquisition and retention of sufficiently skilled personnel to implement and operate the new systems, demands on management time and other risks and costs of delays or difficulties in transitioning to or integrating new systems into our current systems. These implementations, modifications and upgrades may not result in productivity improvements at a level that outweighs the costs of implementation, or at all. In addition, difficulties with implementing new technology systems, delays in our timeline for planned improvements, significant system failures, or our inability to successfully modify our information systems to respond to changes in our business needs may cause disruptions in our business operations and have a material adverse effect on our business, financial condition and results of operations.

Economic conditions may adversely affect our business, financial condition and share price

Adverse worldwide economic conditions may negatively impact our business. A significant change in the liquidity or financial condition of our customers could cause unfavorable trends in their purchases and/or in our receivable collections, and additional allowances may be required, which could adversely affect our business, financial condition and results of operations. Adverse worldwide economic conditions may also adversely impact our suppliers' ability to provide us with materials and components, which could have a material adverse effect on our business, financial condition and results of operations.

The global credit and financial markets have recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, inflation, declines in economic growth, wage inflation because of labor shortages and uncertainty about economic stability. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including the conflict between Russia and Ukraine, terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also adversely impact the financial markets and the global economy, and any economic

countermeasures by affected countries and others could exacerbate market and economic instability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. These developments, or the perception that any of them could occur, may restrict the ability of key market participants to operate in certain financial markets or restrict our access to capital. For example, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our Common Stock.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses

Our operations could be subject to power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, health epidemics or pandemics or other contagious outbreaks, such as the recent COVID-19 pandemic, and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce our products and/or components thereof. Our ability to obtain clinical supplies of our products and/or components thereof could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Disruptions at the FDA, other government agencies and notified bodies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, certified or commercialized in a timely manner or at all, or otherwise prevent those agencies and bodies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business

The ability of the FDA, other government agencies and notified bodies to review and approve or certify new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA’s or other government agencies’ ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA’s, other government agencies’ and notified bodies’ ability to perform routine functions. Average review times at the FDA, other government agencies and notified bodies have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA, other agencies and notified bodies may also slow the time necessary for new drugs and medical devices or modifications to approved drugs or approved or certified medical devices to be reviewed and/or approved or certified by necessary government agencies or notified bodies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA had significantly curtailed and limited its inspection of both foreign and domestic facilities. Furthermore, regulatory authorities outside the United States adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if new or existing global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, in the European Union (the “EU”), notified bodies must be officially designated to certify products and services in accordance with the Medical Devices Regulation (EU) No 2017/745 (the “EU Medical Devices Regulation”). While several notified bodies have been designated, current designated notified bodies are facing a large amount of requests with the new regulation as a consequence of which review times have lengthened. This situation may impact the ability of our notified body(ies) to timely review and process our regulatory submissions, and our ability to grow our business in the EU and European Economic Area (the “EEA”).

We, in conjunction with our partners, intend to expand sales of our products internationally in the future, but we and our partners may experience difficulties in obtaining regulatory approval or certification or in successfully marketing and distributing our products internationally even if approved or certified. A variety of risks associated with marketing and distributing our products internationally could materially adversely affect our business

Our future growth may depend, in part, on our and our partners' ability to develop and commercialize our planned and future products in foreign markets. Sales of our products outside of the United States are and will be subject to foreign regulatory requirements governing clinical studies and marketing approval or certification, as well as FDA regulation of the export of drugs and medical devices from the United States. To obtain separate regulatory approval or certification in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical studies, commercial sales, pricing and distribution of our planned or future products. We and/or our partners will incur substantial expenses in connection with our expected international expansion. Additional risks related to operating in foreign countries include:

- differing reimbursement regimes in foreign countries, including price controls;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- foreign currency fluctuations, which could result in increased operating expenses, reduced revenue and other obligations incidental to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), or comparable foreign regulations;
- the existence of additional third-party patent rights of potential relevance to our business;
- economic weakness, including inflation or political instability in particular foreign economies and markets;
- challenges protecting and enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- product shortages resulting from any events affecting raw material or finished good supply or distribution or manufacturing capabilities abroad;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism (including the ongoing invasion of Ukraine by Russia), natural disasters, including earthquakes, typhoons, floods and fires, or health epidemics or pandemics or other contagious outbreaks, such as the recent COVID-19 pandemic.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations, which would have a material adverse effect on our business, financial condition and results of operations.

In addition, there can be no guarantee that we will receive approval or certification to sell our product candidates in any international market we target, nor can there be any guarantee that any sales would result, even if such approval or certification is received. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities or notified bodies of foreign countries must also approve or certify the manufacturing or marketing of the product candidate in those countries. Approval in the United States, or in any other jurisdiction, does not ensure approval or certification in other jurisdictions. Obtaining foreign approvals or certifications could result in significant delays, difficulties and costs for us and require additional trials and additional expenses. Regulatory requirements can vary widely from country to country and could delay the introduction of our products or product candidates in those countries. Marketing authorization by the FDA does not ensure registration, certification, clearance or approval by regulatory authorities or notified bodies in other countries, and registration, certification, clearance or approval by one or more foreign regulatory authorities or notified bodies does not ensure registration, clearance, certification or approval by regulatory authorities or notified bodies in other foreign countries or by the FDA. However, a failure or delay in obtaining registration or regulatory clearance, certification or approval in one country may have a negative effect on the regulatory process in others. Clinical studies conducted in one country may not be accepted by other countries. If we fail to comply with these regulatory requirements or to obtain and maintain required approvals or certifications, our target market will be reduced and our ability to generate revenue will be diminished. Our inability to successfully enter all our desired international markets and manage business on a global scale could negatively affect our business, financial results and results of operation.

We may in the future bring certain cGMP product release testing, stability testing and cGMP pharmaceutical manufacturing capabilities in-house, and we may not be able to do so successfully or in compliance with FDA regulations

We have brought certain activities that we previously outsourced to third parties, in-house, and we may bring certain additional activities in-house in the future. For example, we have brought certain cGMP product release testing related to SirolimusEFR in-house. In addition, we may eventually bring the manufacture of pharmaceutical drug products, such as SirolimusEFR, in-house. To the extent we do bring these functions in-house, we will be directly subject to FDA and other regulations with respect to these activities, such as the FDA's good laboratory practice requirements, cGMP regulations and similar foreign requirements. We cannot provide assurance that we will be able to perform these functions effectively or comply with applicable regulations if we bring these functions in-house.

We may expend our limited resources to pursue a particular product or indication and fail to capitalize on products or indications that may be more profitable or for which there is a greater likelihood of success

Because we have limited financial and managerial resources, we focus on specific products and product candidates, indications and discovery programs. As a result, we may forgo or delay pursuit of other opportunities with others that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable products. If we do not accurately anticipate physician and patient needs, as well as evaluate the commercial potential or target market for a particular potential product, we may miss valuable product development opportunities or we may relinquish valuable rights to that potential product through future collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to further advance development or to retain sole development and commercialization rights to such potential product.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited

As of December 31, 2022, we had gross net operating loss ("NOL") carryforwards of approximately $108.6 million for federal income tax purposes, and $88.0 million for state income tax purposes, and approximately $3.1 million of federal research and development tax credits, after applying limitations under Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"). Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. Some of these NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We have experienced Section 382 ownership changes in the past, and the federal NOL disclosed above reflects the impact of the calculated Section 382 limitation. In addition, we may experience additional ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership

change has occurred and our ability to use our historical NOLs is materially limited, it could harm our future operating results by effectively increasing our future tax obligations. In addition, under the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), future tax losses may be utilized to offset no more than 80% of the taxable income annually. Under the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act"), signed into law in March 2020, the limitation on the deduction of NOLs to 80% of current year taxable income does not apply to taxable years beginning before January 1, 2021. Federal NOLs arising in taxable years beginning after December 31, 2017 and before January 1, 2021 are required to be carried back to each of the five taxable years preceding the tax year of such loss unless the taxpayer elects to waive or reduce such carryback period, but NOLs arising in taxable years beginning after December 31, 2020 generally may not be carried back. Notwithstanding the CARES Act, we may be required to pay federal income taxes in future years despite generating a loss for federal income tax purposes. There is also a risk that due to statutory or regulatory changes or other unforeseen reasons, our future NOLs could expire or otherwise be unavailable to offset future income tax liabilities. For these reasons, we may not be able to realize a tax benefit from the use of any future NOLs we generate, whether or not we attain profitability. As of December 31, 2022 and June 30, 2023, we recorded a full valuation allowance on our deferred tax assets.

Changes in tax laws could adversely affect the taxes we pay and, as a result, adversely affect our financial condition and results of operations

Tax laws, regulations, and administrative practices may be subject to significant change, with or without notice, due to economic, political and/or other conditions, and significant judgment is required in applying the relevant provisions of tax law. If such changes were to be adopted or if the tax authorities were to challenge our application of relevant provisions of applicable tax laws, our financial condition and results of operations could be adversely affected.

In particular, the U.S. government may enact significant changes to the taxation of business entities including, among others, an increase in the corporate income tax rate, the imposition of minimum taxes or surtaxes on certain types of income, significant changes to the taxation of income derived from international operations, and an addition of further limitations on the deductibility of business interest. For example, the Inflation Reduction Act of 2022 enacted on August 16, 2022, among other provisions, imposes a 15% minimum tax on the adjusted financial statement income of certain large corporations, as well as a 1% excise tax on corporate stock repurchases by publicly traded companies. This act, as well as any other changes to tax laws that are enacted, could adversely affect our tax liability. While certain other draft legislation has been publicly released and is under development in Congress at this time, the likelihood of these changes being enacted or implemented is unclear. We are currently unable to predict whether such changes will occur. If such changes are enacted or implemented, we are currently unable to predict the ultimate impact on our business and therefore there can be no assurance our business will not be adversely affected.

Risks Related to Our Reliance on Third Parties

We are, and expect to continue to be, highly dependent on partners to drive the successful marketing and sale of our initial product candidates. There is no assurance that we will be able to form and properly manage partnerships. There is no assurance that partnerships will be successful

We intend to primarily pursue licensing and distribution arrangements with strategic partners to commercialize and sell our product candidates. As such, licensing and collaboration payments, including upfront and milestone payments, as well as royalties and revenue sharing arrangements related to our products and product candidates, will account for substantially all of our revenue for the foreseeable future. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. We have limited experience in negotiating, establishing and managing such collaborations and we may be unable to successfully form and maintain such arrangements. Without commercialization partners, we may not have adequate financial or other resources to successfully commercialize our product candidates. In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for exclusive rights to commercialize our products or certain rights to control decisions regarding the development and commercialization of our products, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we have entered into or may enter into in the future, or any delay in entering into collaborations related to our products or product candidates, could delay the development and commercialization of our products or product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

Successfully commercializing medical device combinations such as ours is a complex and uncertain process, dependent on the efforts of management, distributors, outside consultants, physicians and general economic conditions, among other factors. Any factors that adversely impact the commercialization of our product candidates will have a negative impact on our business, results of operations and financial condition. We cannot assure you that we or our partners will be successful in developing or commercializing any of our product candidates or any other new product candidates. Our inability to successfully commercialize our product candidates through partnerships and/or successfully develop and commercialize additional products or any enhancements to our products which we may develop would have a material adverse effect on our business, results of operations and financial condition.

We did not meet the target achievement dates relating to certain milestone payments, and we may not meet other target achievement dates relating to additional milestone payments, under our manufacturing and distribution agreement with Terumo, which may have an adverse effect on our relationship with Terumo and our results of operations

In June 2019, we entered into a strategic partnership with Terumo (the “Terumo Partnership”) for the manufacture and distribution of our product candidate Virtue SAB. Under the agreement with Terumo, we were initially eligible for certain milestone payments in the amount of $65 million from Terumo upon completion of certain minimum enrollments in clinical studies, making certain filings and submissions, and obtaining certain regulatory approvals and certifications. Of these milestone payments, $35 million relate to achieving certain milestones by specified target achievement dates, and, as of the date of this prospectus, we have already passed the target achievement dates for two $5 million milestone payments, in each case, without achieving the related milestones. In addition, due to delays in our Virtue SAB program resulting from the COVID-19 pandemic, supply chain issues and unexpected regulatory delays and requirements, we are unlikely to be able to complete the remaining time-based milestones by the specified target achievement dates to earn the remaining $25 million in time-based milestone payments pursuant to our agreement with Terumo. Our failure to earn milestone payments under our agreement with Terumo will have an adverse effect on our results of operations.

Further, Terumo has the right to terminate the agreement, or certain of its obligations thereunder, if certain milestones are not achieved. If Terumo elects to terminate the agreement, our development and commercialization plans for Virtue SAB could be adversely impacted, and this could have a material adverse effect on our business, financial condition, results of operations and prospects.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to our current agreement that could serve to restructure milestone payments as well as make other potential material modifications to that agreement. Until we gain clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development, and commercialization plans for Virtue SAB may continue to be adversely impacted.

We expect to be highly dependent on partners and third-party vendors to manufacture and provide important materials and components for our products and product candidates. There is no assurance that we will be able properly manage our supply chain. Further, we currently do not have redundancy built into our supply chain

We utilize and intend to continue to utilize partners and third-party vendors to assist in the manufacture and assembly of our products and product candidates, as well as to provide materials and components essential to the manufacture of our products and product candidates, in particular Virtue SAB. For example, for our Virtue SAB product candidate, we currently source sirolimus from a single manufacturer in China, and we source angioplasty balloons from a single manufacturer in Singapore. Disruptions in those countries or with respect to those suppliers for any reason, including, without limitation, further outbreaks of COVID-19, including any strains or variants of the virus, or any future pandemic, could cause us to seek new or additional suppliers for these products and could have a material adverse effect on our business.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval, if any. We may be unable to maintain or establish required agreements with third-party manufacturers

or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical study interruptions, or of drug or medical device supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

In addition, successfully manufacturing a medical device combination product or product candidate such as our Virtue SAB is a complex and uncertain process, dependent on the efforts of management, suppliers, manufacturing companies, packaging vendors, testing companies, outside consultants and general economic conditions, among other factors. Our ability to supply our products commercially and to develop any future products depends, in part, on our ability to obtain these materials, components and products in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. Any factors that adversely impact the manufacturing of our products or product candidates will have a negative impact on our business, results of operations and financial condition. We cannot assure you that we or our partners will be successful in manufacturing our current products or product candidates or any potential enhancements to our products or any other new products. Our inability to successfully manufacture our products through partnerships and/or successfully develop and manufacture additional products or any enhancements to our products which we may develop would have a material adverse effect on our business, results of operations and financial condition.

We and our partners may be unable to sustain revenue growth

We expect our ability to increase our revenue in future periods to primarily depend on the ability of commercial partners to successfully penetrate our target markets and increase sales of our products or product candidates, which will, in turn, depend in part on our partners' success in growing their customer base and obtaining reorders from those customers. New products will also need to be developed and approved, or certified or otherwise authorized by the FDA and foreign regulatory agencies or notified bodies to sustain revenue growth in our markets. Additional clinical data and new products may be necessary to grow revenue.

The failure of our manufacturing partners and component suppliers to meet regulatory quality standards applicable to their manufacturing processes could have an adverse effect on our business, financial condition and results of operations

Our medical device and component manufacturers must register with the FDA and are subject to periodic inspection by the FDA for compliance with the FDA's Quality System Regulation ("QSR"), requirements, which require manufacturers of medical devices to adhere to certain manufacturing practices, including design controls, product validation and verification, in process testing, quality control and documentation procedures. Similar requirements apply in foreign jurisdictions. Compliance with applicable regulatory

requirements is subject to continual review and is rigorously monitored through periodic inspections or audits by the FDA and other regulatory agencies or notified bodies. Our component, polymer and drug suppliers are also required to meet certain standards applicable to their manufacturing processes.

We cannot assure you that we, our manufacturing partners, or component suppliers comply or can continue to comply with all regulatory requirements. The inability of one of these parties to achieve or maintain compliance with these requirements or quality standards may disrupt our ability to supply products sufficient to meet demand until compliance is achieved, or until a new supplier or manufacturer has been identified and evaluated. Our or these parties' failure to comply with applicable regulations could cause sanctions to be imposed on us, including warning letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, certifications, license revocation, seizures or recalls of products or product candidates, operating restrictions and criminal prosecutions, which could harm our business. We cannot assure you that if we need to engage new suppliers, manufacturers or testing resources to satisfy our business requirements that we can locate new ones in compliance with regulatory requirements. Our failure to do so could have a material adverse effect on our business, financial condition, results of operations and prospects.

From time to time, we engage outside parties to perform services related to certain of our clinical studies and trials, and any failure of those parties to fulfill their obligations could cause costs and delays

From time to time, we engage consultants and CROs to help design, monitor and analyze the results of certain of our clinical studies and trials. The consultants and CROs we engage interact with clinical investigators to enroll patients in our clinical studies. We depend on these consultants, CROs and clinical investigators to perform the clinical studies and trials and monitor and analyze data from these studies and trials under the investigational plan and protocol for the study or trial and in compliance with regulations and requirements for conducting, recording and reporting results of clinical studies or trials to assure that the data and results are credible and accurate and the trial participants are adequately protected, as required by the FDA and foreign regulatory authorities. The consultants and CROs also are responsible for protecting confidential patient data and complying with U.S. and foreign laws and regulations related to data privacy. We may face delays in our regulatory approval process if these parties do not perform their obligations in a timely or competent fashion or if we must change service providers. This risk is greater for our clinical studies and trials conducted outside of the United States, where it may be more difficult to ensure our studies and trials are conducted in compliance with FDA requirements. Any third parties we hire to design or monitor and analyze results of our clinical studies and trials may also provide services to our competitors, which could compromise the performance of their obligations to us. If these third parties do not successfully carry out their duties or meet expected deadlines, or if the quality, completeness or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical study protocols or for other reasons, our clinical studies or trials may be extended, delayed or terminated or may otherwise prove to be unsuccessful, and our development costs will increase. We may not establish or maintain relationships with these third parties on favorable terms, or at all. If we need to enter into replacement arrangements because a third-party is not performing in accordance with our expectations, we may not be able to do so without undue delays or considerable expenditures, or at all.

The FDA and similar regulatory bodies may hold us responsible for any failure of our third-party consultants or CROs. Our monitoring of our third-party consultants or CROs may fail to detect, remedy or report their failures.

The continuing development of many of our products and product candidates depends upon our maintaining strong working relationships with physicians

The research, development, marketing and sale of many of our new and improved products or product candidates depend upon our maintaining working relationships with physicians. We rely on these professionals to provide us with considerable knowledge and experience regarding the development, marketing and sale of our products or product candidates. Physicians assist us as researchers, marketing and product consultants, inventors and public speakers. If we cannot maintain our strong working relationships with these professionals and continue to receive their advice and input, the development and marketing of our products or product candidates could suffer, which could have a material adverse effect on our business, financial condition, results of operations and prospects. At the same time, the medical device industry's relationship with physicians is under increasing scrutiny by the Office of Inspector General (the "OIG"), and the U.S. Department of Justice (the "DOJ"). Our failure to comply with requirements governing the industry's relationships with physicians, including the reporting of certain payments to physicians under the National Physician Payment Transparency Program or an investigation into our compliance by the OIG or the DOJ, could have a material adverse effect on our business, financial condition, results of operations and prospects.

We have limited pharmaceutical manufacturing experience and our CMOs may experience development or manufacturing problems or delays in producing our products and planned or future products that could limit or prevent the potential growth of our revenue or increase our losses

We are responsible for the manufacture of the proprietary SirolimusEFR used in our Virtue SAB product candidate. We have already experienced substantial delays and other challenges in the manufacture of SirolimusEFR as a result of supply chain and personnel issues experienced by the single source CMO that produces SirolimusEFR for us. Many of the processes, ingredients and components required for manufacture of SirolimusEFR are also required for manufacture of COVID-19 vaccines and tests and, as such, supply chains continue to be adversely impacted. Further, the manufacture of SirolimusEFR involves certain novel processes that we continue to develop to achieve consistent reproducibility as well as increase scale to support large clinical studies and future commercialization. In the event that we do not have sufficient SirolimusEFR, our planned clinical studies could be prevented or delayed. Further delays in our trial timelines will result in additional expenses to us and potentially risk or damage our partnership with Terumo and the future competitiveness of our Virtue SAB solution.

If approved for use in connection with our medical device product candidates or as a stand-alone product, we currently expect to remain responsible for the manufacture and supply of SirolimusEFR at clinical and/or commercial scale for our partner, Terumo. We have limited experience in manufacturing pharmaceutical products and no experience manufacturing SirolimusEFR in the volume that we anticipate will be required if we achieve planned levels needed for clinical studies and/or commercial sales. We do not currently have, nor do we currently have plans to acquire, the infrastructure or capability internally to manufacture or test SirolimusEFR on a clinical and/or commercial scale. Instead, we rely on contract manufacturers for current production of SirolimusEFR for clinical study supplies and currently plan to continue to use contract manufacturers for supply and testing. Our reliance on third-party suppliers and manufacturers, including certain single-source suppliers, could harm our ability to fulfill our supply obligations to Terumo. If our third-party suppliers fail to deliver the required quantities of materials on a timely basis and at reasonable prices, and we are unable to find one or more replacement suppliers capable of production at a substantially equivalent cost in substantially equivalent volumes and quality on a timely basis, the supply of our products or product candidates to customers and the development of any future products will be delayed, limited or prevented, which could have material adverse effect on our business, financial condition and results of operations.

The facilities used by our CMOs to manufacture our product candidates must be authorized by the applicable regulatory authorities, including the FDA, pursuant to inspections that will be conducted after a PMA, New Drug Application (“NDA”) or comparable foreign regulatory marketing application is submitted. We do not control the manufacturing process of our product candidates and are completely dependent on our contract manufacturing partners for compliance with the FDA’s cGMP or similar foreign requirements for manufacture of both the active drug substances and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA’s or foreign regulatory authorities’ strict regulatory requirements, they will not be able to secure or maintain FDA or foreign approval for use of their manufacturing facilities with respect to our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, without delay, or at all, which would significantly impact our ability to fulfill our supply obligations for SirolimusEFR for Virtue SAB, as well as sales of SirolimusEFR for other potential clinical applications.

In addition, the manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. They may also encounter equipment breakdowns requiring lengthy repairs or the need to replace equipment. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in our supply or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination and could require that affected supplies be withdrawn or withheld from the market. Any stability or other issues relating to the manufacture of our product candidates may occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with

their contractual obligations, our ability to provide SirolimusEFR to Terumo would be jeopardized, which would result in a material adverse effect on our business, financial condition, results of operations and prospects.

Reduction or interruption in supply and an inability to develop alternative sources for supply may adversely affect our partners' manufacturing operations and related product sales

We purchase many of the components and raw materials used in manufacturing our products from numerous suppliers in various countries. Generally, we have been able to obtain adequate supplies of such raw materials and components. However, for reasons of quality assurance, cost-effectiveness or availability, we may procure certain components and raw materials from a sole supplier. For example, for our Virtue SAB product candidate, we source sirolimus from a single manufacturer in China, we source angioplasty balloons from a single manufacturer based in Ireland that uses a production facility based in Singapore to manufacture balloons for us, and we source custom polymers from a single manufacturer in the United States. We work closely with our suppliers to try to ensure continuity of supply while maintaining high quality and reliability. However, we cannot guarantee that these efforts will be successful. In addition, due to the stringent regulations and requirements of the FDA, comparable regulatory bodies in countries in the EU and similar regulatory bodies elsewhere around the world regarding the manufacture of our products or product candidates, we may not be able to quickly establish additional or replacement sources for certain components or materials. A reduction in or an interruption to supply, and an inability to develop alternative sources for such supply, could adversely affect our ability to manufacture our products in a timely or cost-effective manner and to make our related product sales. Manufacturing facilities used to make our balloons or other components may be shut down, sold or otherwise become unavailable and it will take time and money for us to identify and requalify new facilities.

In addition, assuming our BackBeat CNT product candidate is approved, we will be reliant on Medtronic, Inc. (an affiliate of Medtronic plc) ("Medtronic") and its ability to obtain supplies for and to produce its BackBeat CNT-enabled pacemaker systems. If Medtronic is unable or unwilling to obtain such supplies or is otherwise unable or unwilling to produce its BackBeat CNT-enabled pacemaker systems, it could adversely affect our results of operations.

We source certain products from foreign suppliers, making us vulnerable to supply problems or price fluctuations caused by trade conflicts and other geopolitical events

Geopolitical risks and other global events could negatively affect our ability to rely on foreign suppliers. Ongoing uncertainty in the trade relationship between China and the United States could cause delays in the manufacturing supply chain for sirolimus, which we currently source from China. Likewise, export restrictions enacted in foreign countries as a result of the COVID-19 pandemic or any future pandemic, including those imposed in China, could limit our ability to obtain products from foreign suppliers or make foreign-made products more costly than anticipated. Any disruptions or delays in our supply chain could negatively impact our ability to operate our business or increase our costs. Further, any tariffs imposed on products we or our partners import from China, Singapore or any other foreign supplier, as a result of global trade conflict, could cause us to increase prices for our future products or reduce our margins.

In February 2022, following Russia's invasion of Ukraine, the United States and the EU imposed various economic sanctions against Russia. If Russia responds with retaliatory measures such as restrictions on the sale of oil or other energy resources from Russia to other countries in the region, that could result in an increase in our global shipping expenses, reduce our sales or otherwise have an adverse effect on our European operations. Additionally, escalation by Russia beyond Ukraine and into other countries within the region could also reduce our sales and have a negative effect on our European operations.

Risks Related to Government Regulation and Our Industry

Healthcare reform initiatives and other administrative and legislative proposals may adversely affect our business

There have been, and continue to be, proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of healthcare and, more generally, to reform the U.S. healthcare system. Certain of these proposals could limit the prices we are able to charge for our products or the coverage and reimbursement available for our products and could limit the acceptance and availability of our products. The adoption of proposals to control prices could have a material adverse effect on our business, financial condition, results of operations and prospects.

In the United States, there have been, and continue to be a, number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and the Affordable Care Act, as amended by the Health Care and Education and Reconciliation Act (collectively, the “ACA”) was enacted in the United States, which made a number of substantial changes in the way healthcare is financed by both governmental and private insurers. Among other ways in which it may affect our business, the ACA established a new Patient-Centered Outcomes Research Institute to oversee and identify priorities in comparative clinical effectiveness research in an effort to coordinate and develop such research, implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other healthcare providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models, and expanded the eligibility criteria for Medicaid programs.

Since its enactment, there have been judicial, U.S. Congressional and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court’s decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, reduced Medicare payments to providers, effective on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2031, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 (the “MACRA”), enacted on April 16, 2015, repealed the formula by which Medicare made annual payment adjustments to physicians and implemented fixed annual updates and a new system of incentive payments that began in 2019 that are based on various performance measures and physicians’ participation in alternative payment models such as accountable care organizations. It is unclear what effect new quality and payment programs, such as MACRA, may have on our business, financial condition, results of operations or cash flows.

In addition to continuing pressure on prices and cost-containment measures in the United States, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We expect additional state, federal and foreign healthcare policies and reform measures to be adopted in the future, any of which could limit reimbursement for healthcare products and services or otherwise result in reduced demand for our products or other products we may commercialize in the future or additional pricing pressure and have a material adverse effect on our industry generally and on our customers. Any changes in, or uncertainty with respect to, future coverage or reimbursement rates could affect demand for our products or other products we may commercialize in the future, which, in turn, could impact our ability to successfully commercialize our products or other products we may commercialize in the future and could have a material adverse effect on our business, financial condition and results of operations.

For instance, in December 2021, the EU Regulation No 2021/2282 on Health Technology Assessment (the “HTA”), amending Directive 2011/24/EU, was adopted. This regulation, which entered into force in January 2022, intends to boost cooperation among EU member states in assessing health technologies, including some medical devices, and providing the basis for cooperation at the EU

level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

Regulatory compliance is expensive, complex and uncertain, and approvals or certifications can often be denied or significantly delayed. We may not obtain the necessary approvals or certifications and failure to obtain timely regulatory approval or certification, if at all, would adversely affect our business

We are not permitted to commercialize, market, promote or sell any of our product candidates in the United States without obtaining approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval or certification by the FDA, comparable foreign regulatory authorities and notified bodies is unpredictable, typically takes many years following the commencement of clinical studies and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions, which may cause delays in the approval, certification or the decision not to approve an application. Regulatory authorities and notified bodies have substantial discretion in the approval or certification process and may refuse to accept any application or may decide that our data are insufficient for approval or certification and require additional preclinical, clinical or other studies. We have not submitted for or obtained marketing approval for any product candidate, except for European Conformity (“CE”) mark certification of our first-generation BackBeat CNT on the Moderato implantable pulse generator (“IPG”) device.

In the United States, before we can market a new medical device, or a new use of, new claim for or significant modification to an existing device, we must first receive either clearance under Section 510(k) of the Federal Food, Drug, and Cosmetic Act (the “FDCA”), or approval of a PMA application from the FDA, unless an exemption applies. Under the FDCA, medical devices are classified into one of three classes, Class I, Class II or Class III, depending on the degree of risk associated with each medical device and the extent of manufacturer and regulatory control needed to ensure its safety and effectiveness. Certain Class I and Class II devices are exempt from premarket notification (510(k)) requirements as well as the Medical Device cGMPs, also referred to as the QSR. A Class I or Class II device that is exempt from 510(k) requirements must still comply with other requirements unless the device is explicitly exempt from those requirements as indicated in the regulation for that device type. We do not believe Virtue SAB or BackBeat CNT or other of our current product candidates will be exempt from, or eligible for, clearance under Section 510(k) of the FDCA. We expect our product candidates will require submission and FDA approval of a PMA to be marketed in the United States. In the process of obtaining PMA approval, the FDA must determine that a proposed device is safe and effective for its intended use(s) based, in part, on extensive data, including, but not limited to, technical, preclinical, clinical study, manufacturing and labeling data. The PMA process is typically required for devices that are deemed to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices. Modifications to products that are approved through a PMA application generally require FDA approval. The PMA process can be expensive, lengthy and uncertain. The process of obtaining a PMA is much more costly and uncertain than the 510(k) clearance process and generally takes from one to three years, or even longer, from the time the application is submitted to the FDA.

In the United States, before we can market a new drug product, or market an approved drug for a new indication, we must receive approval of an NDA. In the process of obtaining NDA approval, the FDA must determine that the drug product candidate is safe and effective for its intended uses. The NDA is a comprehensive, multivolume application that includes, among other things, the results of preclinical and clinical studies, information about the drug’s composition, and plans for manufacturing, packaging and labeling the drug. The time required to obtain NDA approval by the FDA is unpredictable and typically takes many years following the commencement of clinical studies.

We expect that obtaining regulatory approvals for our product candidates will require us to conduct human clinical studies. For our medical device product candidates and combination drug/device product candidates regulated as medical devices, we will need to obtain approval of an investigational device exemption (“IDE”), prior to beginning a clinical study in the United States. For our drug product candidates, we will need to submit an investigational new drug (“IND”) application that the FDA authorizes prior to beginning clinical studies in the United States. Preclinical studies, submissions related to chemistry, manufacturing and controls

("CMC") of our product candidates, and safety data such as biocompatibility will be required in connection with any IDE or IND applications. It is possible that unforeseen failure of one or more of these tests could cause delays in the application process.

Despite the time, effort and cost involved in conducting clinical studies and seeking regulatory approvals or certifications, a product candidate may not be approved or certified by the FDA or comparable regulatory authorities or notified bodies. Any delay or failure to obtain necessary regulatory approvals or certifications could harm our business. Furthermore, even if we are granted regulatory approvals or certifications, they may include significant limitations on the indicated uses for the device, which may limit the market for the product.

The FDA, comparable regulatory authorities (or notified bodies) can delay, limit or deny approval of a drug or approval or certification of a medical device for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable regulatory entity or notified body that our products are safe or effective for their intended uses;
- inability to satisfy regulators on the biocompatibility of our novel materials or to gain agreement with regulators on the methods or results of biocompatibility testing;
- the disagreement of the FDA or the applicable foreign regulatory authority or notified body with the design or implementation of our clinical studies or the interpretation of data from preclinical studies or clinical studies;
- serious and unexpected adverse effects experienced by participants in our clinical studies;
- the data from our preclinical studies and clinical studies may be insufficient to support approval;
- our inability to demonstrate that the clinical and other benefits of the product candidate outweigh the risks;
- the quality systems, manufacturing processes and/or facilities we use may not meet applicable requirements; and
- the potential for approval policies or regulations of the FDA or applicable foreign regulatory bodies to change significantly in a manner rendering our clinical data or regulatory filings insufficient for approval or certification.

The regulations to which we are subject are complex and have tended to become more stringent over time. Regulatory changes could result in restrictions on our ability to carry on or expand our operations, higher than anticipated costs or lower than anticipated sales. The FDA and foreign regulatory authorities enforce these regulatory requirements through various mechanisms, including periodic unannounced inspections. We do not know whether we or any CMOs we may utilize will pass any future FDA, foreign regulatory authorities or notified bodies inspections or audits. Failure to comply with applicable regulations could jeopardize our ability to sell our products and result in enforcement actions such as: warning letters; fines; injunctions; civil penalties; termination of distribution; recalls or seizures of products; delays in the introduction of products into the market; total or partial suspension of production; refusal to grant future approvals or certifications; withdrawals or suspensions of current approvals or certifications, resulting in prohibitions on sales of our products; and, in the most serious cases, criminal penalties.

Subject to the transitional provisions provided in the EU Medical Devices Regulation, and in order to sell our products in EU member states, our products must comply with the general safety and performance requirements of the EU Medical Devices Regulation, which repeals and replaces the Medical Devices Directive and the Active Implantable Medical Devices Directive. Compliance with these requirements is a prerequisite to be able to affix the CE mark to our products, without which they cannot be sold or marketed in the EU. All medical devices (including active implantable medical devices) placed on the market in the EU must meet the general safety and performance requirements laid down in Annex I to the EU Medical Devices Regulation, including the requirement that a medical device must be designed and manufactured in such a way that, during normal conditions of use, it is suitable for its intended purpose. Medical devices must be safe and effective and must not compromise the clinical condition or safety of patients, or the safety and health of users and — where applicable — other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. To demonstrate compliance

with the general safety and performance requirements, we must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. A conformity assessment procedure generally requires the intervention of a notified body. The notified body would typically audit and examine the technical file and the quality system for the manufacture, design and final inspection of our devices. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EU. If we fail to comply with applicable laws and regulations, we would be unable to affix the CE mark to our products, which would prevent us from selling them within the EU.

The aforementioned EU rules are generally applicable in the EEA (which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland). Non-compliance with the above requirements would also prevent us from selling our products in these countries.

International regulatory approval or certification processes may take longer than the FDA approval process. If we fail to comply with applicable FDA and foreign regulatory requirements, we may not receive regulatory approvals or certifications or may be subject to FDA or foreign enforcement actions. We may be unable to obtain future regulatory approval or certification in a timely manner, or at all, especially if existing regulations are changed or new regulations are adopted. A failure or delay in obtaining necessary regulatory approvals or certifications would materially adversely affect our business.

In the EU, we must inform the notified body that carried out the conformity assessment of the medical devices that we market or sell in the EU and the EEA of any planned substantial changes to our quality system or substantial changes to our medical devices that could affect compliance with the general safety and performance requirements laid down in Annex I to the EU Medical Devices Regulation or cause a substantial change to the intended use for which the device has been CE marked. The notified body will then assess the planned changes and verify whether they affect the products' ongoing conformity with the EU Medical Devices Regulation. If the assessment is favorable, the notified body will issue a new certificate of conformity or an addendum to the existing certificate attesting compliance with the general safety and performance requirements and quality system requirements laid down in the Annexes to the EU Medical Devices Regulation. The notified body may disagree with our proposed changes and product introductions or modifications could be delayed or canceled, which could adversely affect our ability to grow our business.

Our medical device products must be manufactured in accordance with federal, state and foreign regulations, and we or any of our suppliers or third-party manufacturers could be forced to recall our installed systems or terminate production if we fail to comply with these regulations

The methods used in, and the facilities used for, the manufacture of our medical device products must comply with the FDA's QSR which is a complex regulatory scheme that covers the procedures and documentation of the design, testing, production, process controls, quality assurance, labeling, packaging, handling, storage, distribution, installation, servicing and shipping of medical devices. Furthermore, we are required to verify that our suppliers maintain facilities, procedures and operations that comply with our quality standards and applicable regulatory requirements. The FDA enforces the QSR through periodic announced or unannounced inspections of medical device manufacturing facilities, which may include the facilities of subcontractors. Our products are also subject to similar state regulations and various laws and regulations of foreign countries governing manufacturing. Our third-party manufacturers may not take the necessary steps to comply with applicable regulations, which could cause delays in the delivery of our products. In addition, failure to comply with applicable FDA or foreign regulatory requirements or later discovery of previously unknown problems with our products or manufacturing processes could result in, among other things: warning letters or untitled letters; fines, injunctions or civil penalties; suspension or withdrawal of approvals; seizures or recalls of our products; total or partial suspension of production or distribution; administrative or judicially imposed sanctions; the FDA's, foreign regulatory authorities' or notified bodies' refusal to grant pending or future approvals or certifications for our product candidates; clinical holds; refusal to permit the import or export of our product candidates; and criminal prosecution of us or our employees.

Any of these actions could significantly and negatively affect supply of our products. If any of these events occurs, our reputation could be harmed, we could be exposed to product liability claims and we could lose customers and experience reduced sales and increased costs.

Even if we obtain regulatory approval or certification for a product candidate, our products will remain subject to regulatory scrutiny and post-marketing requirements. Failure to comply with post-marketing regulatory requirements could subject us to enforcement actions, including substantial penalties, and might require us to recall or withdraw a product from the market

Any regulatory approvals or certifications that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our drug product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if one of our product candidates is approved or certified, it will be subject to ongoing and pervasive regulatory requirements governing, among other things, the manufacture, marketing, labeling, advertising, adverse event reporting, recordkeeping, sale, promotion, sampling, testing, conduct of post-marketing studies, registration, and listing of drugs and medical devices. For example, we must submit periodic reports to the FDA as a condition of approval. These reports include safety and effectiveness information about the drug or device after its approval. Failure to submit such reports, or failure to submit the reports in a timely manner, could result in enforcement action by the FDA. Following its review of the periodic reports, the FDA might ask for additional information or initiate further investigation.

The regulations to which we are subject are complex and have become more stringent over time. Regulatory changes could result in restrictions on our ability to continue or expand our operations, higher than anticipated costs or lower than anticipated sales. Even after we have obtained the proper regulatory approval or certification to market a device, we have ongoing responsibilities under FDA regulations and applicable foreign laws and regulations. The FDA, state and foreign regulatory authorities have broad enforcement powers. Our failure to comply with applicable regulatory requirements could result in enforcement action by the FDA, state or foreign regulatory authorities, which may include any of the following sanctions:

- untitled letters or warning letters;
- fines, injunctions, consent decrees and civil penalties;
- recalls, termination of distribution, administrative detention or seizure of our products;
- customer notifications or repair, replacement or refunds;
- operating restrictions or partial suspension or total shutdown of production;
- delays in or refusal to grant our requests for future PMA approvals or foreign regulatory approvals or certifications of new products, new intended uses or modifications to existing products;
- withdrawals or suspensions of our current PMA or foreign regulatory approvals or certifications, resulting in prohibitions on sales of our products;
- FDA refusal to issue certificates to foreign governments needed to export products for sale in other countries; and
- criminal prosecution.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval or certification is withdrawn, our business will be seriously harmed.

Moreover, the policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval or certification of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action,

either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval or certification that we may have obtained and we may not achieve or sustain profitability.

Modifications to any approved or certified device products may require us to obtain new PMA approvals or approvals of a PMA supplement or foreign certification, and if we market modified products without obtaining necessary approvals or certifications, we may be required to cease marketing or recall the modified products until required approvals or certifications are obtained

Certain modifications to any device product for which we receive PMA approval may require approval of a new PMA or a PMA supplement, or alternatively a notification or other submission to the FDA. The FDA requires device manufacturers to make and document a determination of whether a modification requires an approval, supplement or clearance; however, the FDA can review a manufacturer's decision. The FDA may not agree with our decisions regarding whether approval of a modification is necessary. We may make modifications to approved devices in the future that we believe do not require approval of a new PMA or PMA supplement. If the FDA disagrees with our determination and requires us to submit a new PMA or PMA supplement for modifications to our previously approved device products, we may be required to cease marketing or to recall the modified product until we obtain approval, and we may be subject to significant regulatory fines or penalties. In addition, the FDA may not approve our products for the indications that are necessary or desirable for successful commercialization or could require clinical trials to support any modifications. Any delay or failure in obtaining required approvals would adversely affect our ability to introduce new or enhanced products in a timely manner, which, in turn, would harm our future growth.

In the EU, we must inform the notified body that carried out the conformity assessment of the medical devices that we market or sell in the EU and the EEA of any planned substantial changes to our quality system or substantial changes to our medical devices that could affect compliance with the general safety and performance requirements laid down in Annex I to the EU Medical Devices Regulation or cause a substantial change to the intended use for which the device has been CE marked. The notified body will then assess the planned changes and verify whether they affect the products' ongoing conformity with the EU Medical Devices Regulation. If the assessment is favorable, the notified body will issue a new certificate of conformity or an addendum to the existing certificate attesting compliance with the general safety and performance requirements and quality system requirements laid down in the Annexes to the EU Medical Devices Regulation. The notified body may disagree with our proposed changes and product introductions or modifications could be delayed or canceled, which could adversely affect our ability to grow our business.

Our medical device products, if approved or certified, may cause or contribute to adverse medical events or be subject to failures or malfunctions that we are required to report to the FDA or similar foreign regulatory authorities, and if we fail to do so, we would be subject to sanctions that could harm our reputation, business, financial condition and results of operations. The discovery of serious safety issues with our products, or a recall of our products either voluntarily or at the direction of the FDA or another governmental authority, could have a negative impact on us

We are subject to the FDA's medical device reporting regulations and similar foreign regulations, which require us to report to the FDA when we receive or become aware of information that reasonably suggests that one or more of our products may have caused or contributed to a death or serious injury or malfunctioned in a way that, if the malfunction were to recur, it could cause or contribute to a death or serious injury. The timing of our obligation to report is triggered by the date we become aware of the adverse event, as well as the nature of the event. We may fail to report adverse events of which we become aware within the prescribed timeframe. We may also fail to recognize that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of the product. If we fail to comply with our reporting obligations, the FDA or foreign regulatory authorities could take action, including warning letters, untitled letters, administrative actions, criminal prosecution, imposition of civil monetary penalties, revocation of our device approval, seizure of our products or delay in approval or certification of future products.

The FDA and foreign regulatory bodies have the authority to require the recall of commercialized products in the event of material deficiencies or defects in design or manufacture of a product or in the event that a product poses an unacceptable risk to health. The FDA's authority to require a recall must be based on a finding that there is reasonable probability that the device could cause serious injury or death. We may also choose to voluntarily recall a product if any material deficiency is found. A government-mandated or voluntary recall by us could occur as a result of an unacceptable risk to health, component failures, malfunctions, manufacturing defects, labeling or design deficiencies, packaging defects or other deficiencies or failures to comply with applicable regulations. Product defects or other errors may occur in the future.

Depending on the corrective action we take to redress a product's deficiencies or defects, the FDA, foreign regulatory authorities or notified bodies may require, or we may decide, that we will need to obtain new approvals or certifications for the device before we may market or distribute the corrected device. Seeking such approvals or certifications may delay our ability to replace the recalled devices in a timely manner. Moreover, if we do not adequately address problems associated with our devices, we may face additional regulatory enforcement action, including FDA and similar foreign regulatory authorities warning letters, product seizure, injunctions, administrative penalties or civil or criminal fines.

Companies are required to maintain certain records of recalls and corrections, even if they are not reportable to the FDA. We may initiate voluntary withdrawals or corrections for our products in the future that we determine do not require notification of the FDA or foreign regulatory authorities. If the FDA or foreign regulatory authorities disagree with our determinations, it could require us to report those actions as recalls and we may be subject to enforcement action. A future recall announcement could harm our reputation with customers, potentially lead to product liability claims against us and negatively affect our sales. Any corrective action, whether voluntary or involuntary, as well as defending ourselves in a lawsuit, will require the dedication of our time and capital, distract management from operating our business and may harm our reputation and financial results.

Virtue SAB is a drug/device combination, which may result in additional regulatory and other risks

Our Virtue SAB product candidate is subject to regulation in the United States as a drug/device combination product. If marketed individually, each component of Virtue SAB would be subject to different regulatory pathways and would require approval of independent marketing applications by the FDA. A combination product, however, is assigned to an FDA center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic effect. In the case of Virtue SAB, we believe that the primary mode of action is attributable to the device component of the product. In this regard, in 2019, the FDA confirmed that Virtue SAB will be regulated as a combination product candidate, with the FDA's Center for Devices and Radiological Health as the lead review center of a marketing application. The determination of whether a combination product requires a single marketing application or two separate marketing applications for each component is made by the FDA on a case-by-case basis. Although we believe a single marketing application for the approval of a combination product would be successful, there can be no assurance that the FDA will not determine that separate marketing applications are necessary. If the FDA were to make that determination, it could significantly increase the resources and time required to bring a particular combination product to market.

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. For instance, drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. In such a case, the marketing authorization application must include — where available — the results of the assessment of the conformity of the device part with the EU Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the marketing authorization application does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the EMA or the EU member state competent authority must require the applicant to provide a notified body opinion on the conformity of the device. By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are, e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the EU Medical Devices Regulation.

Although the FDA and similar foreign regulatory agencies have or may have systems in place for the review and approval or certification of combination products such as ours, we have and may continue to experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process, as well as coordination between two different centers within FDA responsible for review of the different components of the combination product.

If the FDA does not conclude that SirolimusEFR as a standalone product candidate satisfies the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for SirolimusEFR under Section 505(b)(2) are not as we expect, the approval pathway for SirolimusEFR may take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful

We may seek FDA approvals for our SirolimusEFR as both a standalone drug product candidate and as part of our Virtue SAB product candidate as well as, potentially, other device/drug combination product candidates for other clinical applications. For the standalone drug product candidate development program, we may seek approval for SirolimusEFR to treat conditions such as ophthalmic inflammatory disease (uveitis) and acute or chronic joint inflammation (osteoarthritis), through the Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from trials that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if we are eligible to pursue such a marketing application, would allow an NDA we submit to the FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved drugs, which could expedite the development program for our product candidates by potentially decreasing the amount of clinical data that we would need to generate in order to obtain FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as we anticipate, we may need to conduct additional clinical studies, provide additional data and information and meet additional standards to obtain regulatory approval, if ever. If this were to occur, the time and financial resources required to obtain FDA approval for SirolimusEFR, and complications and risks associated with the development of certain of our product candidates, would likely substantially increase. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in competitive products reaching the market before our product candidates, which could impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization, or that a competitor would not obtain approval first along with subsequent market exclusivity from the FDA, thereby delaying potential approval of our product.

In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to expedited product development or earlier approval.

Moreover, even if our product candidates are approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. For instance, drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. In such a case, the marketing authorization application must include — where available — the results of the assessment of the conformity of the device part with the EU Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the marketing authorization application does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the European Medicines Agency ("EMA") or the EU member state competent authority must require the applicant to provide a notified body opinion on the conformity of the device. By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are, e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the EU Medical Devices Regulation. Should SirolimusEFR be considered a drug product, it would be subject to various other EMA regulatory requirements and timelines.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay

As product candidates proceed through preclinical studies to late-stage clinical studies towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the timing, continuation or results of planned clinical studies or other future clinical studies conducted with the altered materials. Such changes may also require additional testing and/or FDA or foreign regulatory authority approval or notified body certification. This could delay completion of clinical studies, require the conduct of bridging clinical studies or the repetition of one or more clinical studies, increase clinical study costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

Our relationships with physicians, patients and payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, and other healthcare laws and regulations

Our current and future operations with respect to the commercialization of our products are subject to various U.S. federal, state and foreign healthcare laws and regulations. These laws will affect our operations, sales and marketing activities, support and education programs and our relationships with physicians and other customers and third-party payors. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation;

- the federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;

- the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 1996 ("HIPAA"), which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners (manufacturers are required to submit reports to the government by the 90th day of each calendar year); and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government;

and state and foreign laws that require drug and medical device manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. Certain physicians who may be in a position to influence the ordering or use of our products in procedures they perform have ownership interests in us and/or receive compensation for consulting and advisory services provided to us. It is possible that governmental authorities will conclude that our business practices do not comply with applicable fraud and abuse or other healthcare laws and regulations or guidance. If our operations are found to be in violation of such laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Healthcare cost-containment pressures and legislative or administrative reforms resulting in restrictive coverage and reimbursement practices of third-party payors could decrease the demand for our products, the prices that customers are willing to pay for those products and the number of procedures performed using our devices, which could have an adverse effect on our business

Our products are, and our future products are expected to be, purchased principally by hospitals and ambulatory medical facilities, which typically bill various third-party payors, including governmental programs, such as Medicare and Medicaid, private insurance plans and managed care plans, for the healthcare services provided to their patients. Because there is often no separate reimbursement for products used in surgical procedures, the additional cost associated with the use of some of our products can impact the profit margin of the hospital or surgery center where the procedure is performed. Some of our target customers may be unwilling to adopt our products in light of the additional associated cost. Further, any decline in the amount payors are willing to reimburse our customers for the procedures using our products may make it difficult for customers to adopt our products and could create additional pricing pressure for us. We may be unable to sell our products on a profitable basis if third-party payors deny coverage or reduce their current levels of reimbursement. The ability of our customers to obtain appropriate coverage and reimbursement for our products or procedures using our products from government and private third-party payors is critical to our success.

Reimbursement varies from country to country, state to state and plan to plan, and can significantly influence the acceptance of new products and services. Certain private third-party payors may view some procedures using our products as experimental and may not provide coverage. Third-party payors may not cover and reimburse the procedures using our products in whole or in part in the future, or payment rates may not be adequate, or both. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. Further, the adequacy of coverage and reimbursement by third-party payors is also related to billing codes to describe procedures performed using our products. Hospitals and physicians use several billing codes to bill for such procedures. Third-party payors may not continue to recognize the billing codes available for use by our customers.

Reimbursement rates are unpredictable, and we cannot project how our business may be affected by future legislative and regulatory developments. Future legislation or regulation, or changing payment methodologies, may have a material adverse effect on our business, and reimbursement may not be adequate for all customers. From time to time, typically on an annual basis, payment amounts are updated and revised by third-party payors. Because the cost of our products generally is recovered by the healthcare provider as part of the payment for performing a procedure and not separately reimbursed, these updates could directly impact the demand for our products. We cannot predict how pending and future healthcare legislation will impact our business and any changes in coverage and reimbursement that further restricts coverage of our products or lowers reimbursement for procedures using our devices could materially affect our business.

After we develop new products or seek to market our products for new indications, once approved (or certified), we may find limited demand for the product unless government and private third-party payors provide adequate coverage and reimbursement. Even with reimbursement approval and coverage by government and private payors, providers submitting reimbursement claims may face delays in payment if there is confusion by providers regarding the appropriate codes to use in seeking reimbursement. Such delays may create an unfavorable impression within the marketplace regarding the level of reimbursement or coverage available for our products.

Demand for our products or new approved (or certified) indications for our existing products may fluctuate over time if federal, state and foreign legislative or administrative policy changes affect coverage or reimbursement levels for our products, or the services related to our products. In the United States, there have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system, some of which could significantly affect our business. Legislative or administrative reforms to the U.S. or international reimbursement systems in a manner that significantly reduces reimbursement for procedures using our medical devices or denies coverage for those procedures could have a material adverse effect on our business, financial condition, results of operations and prospects.

Actual or perceived failures to comply with U.S. and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and financial performance

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical studies in the United States and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or our collaborators', service providers' and contractors' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, imposes privacy, security and breach notification obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities, and their covered subcontractors. HIPAA establishes privacy and security standards that limit the use and disclosure of individually identifiable health information and protected health information ("PHI") and requires the implementation of administrative, physical and technological safeguards to protect the privacy of PHI and ensure the confidentiality, integrity and availability of electronic PHI. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. Covered entities are those that electronically transmit health information in connection with transactions susceptible to standards set by the U.S. Department of Health and Human Services ("HHS") and may concern billing and payment for services or insurance coverage. Business associates may perform or assist in performance of a function or activity involving the use or disclosure of individually identifiable health information, or other activities that may involve disclosure of individually identifiable health information by the covered entity. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and, thus, are not directly regulated under HIPAA, federal and state regulators may disagree and bring an enforcement action under HIPAA against us.

In addition, certain state laws govern the privacy and security of health-related and other personal information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. By way of example, the California Consumer Privacy Act (the "CCPA"), which went into effect on January 1, 2020, gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, the California Privacy Rights Act (the "CPRA") recently passed in California. The CPRA significantly amends the CCPA and will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging.

In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, the EU and the UK General Data Protection Regulations (respectively, the "EU GDPR" and the "UK GDPR," together, the "GDPR**")** each impose strict requirements for processing the personal data of individuals within the EEA, and/or the UK and to processing that occurs in the context of an establishment in, respectively, the EEA and/or UK. The EU GDPR, which went into effect in May 2018 and introduces strict requirements for processing the personal information of EU subjects, including clinical study data. The GDPR has and will continue to increase compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and process information about them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million under the EU GDPR and £17.5 million under the UK GDPR or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition to these fines, supervisory authorities have extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors; the GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR.

The existence of parallel regimes under the EU GDPR and UK GDPR, and divergence in respect of implementing or supplementary laws across the EEA and UK in certain areas, means that we could be subject to potentially overlapping or divergent enforcement actions for certain actual or perceived violations. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July 2020, the Court of Justice of the EU, (the "CJEU"), limited how organizations could lawfully transfer personal data from the EEA and UK to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("SCCs"). The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements had to be migrated to the revised clauses by December 27, 2022. The revised SCCs cannot be used for transfers to non-EEA entities whose processing is already subject to the GDPR; however, no equivalent standard data protection clauses have been issued and approved by the European Commission and, therefore, current market practice is largely to use the SCCs notwithstanding this issue. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK. The UK's Information Commissioner's Office has published new data transfer standard contracts for transfers from the UK under the UK GDPR. This new documentation became mandatory for relevant data transfers from September 21, 2022; existing standard contractual clauses arrangements must be migrated to the new documentation by March 21, 2024. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and the European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews or extends that decision. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit and the response to this consultation was published in June 2022. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision and the UK losing its adequacy decision if the European Commission deems the UK no longer provides adequate protection of personal data.

As supervisory authorities issue further guidance on personal data export mechanisms, including the aforementioned 'supplementary measures,' and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations. The GDPR may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms, at significant cost and diversion of management attention, to ensure compliance with the new data protection rules. This may be onerous and may adversely affect our business, operations and financial performance.

The EU has also proposed a Regulation on Privacy and Electronic Communications, or ePrivacy Regulation, which, if adopted, would impose new obligations on the use of personal data in the context of electronic communications, particularly with respect to online tracking technologies and direct marketing. Additionally, the EU adopted the EU Clinical Trials Regulation, which came into effect on January 31, 2022. This regulation imposes new obligations on the use of data generated from clinical trials and enables European patients to have the opportunity to access information about clinical trials. Failure or perceived failure to comply with the GDPR, the EU Clinical Trials Regulations or other countries' privacy or data security-related laws, rules or regulations could result in significant regulatory penalties and fines, affect our compliance with contracts entered into with our partners, collaborators and other third-party payors, and could have an adverse effect on our reputation, business and financial condition.

Environmental and health safety laws may result in liabilities, expenses and restrictions on our operations

Federal, state, local and foreign laws regarding environmental protection, hazardous substances and human health and safety may adversely affect our business. Using hazardous substances in our operations exposes us to the risk of accidental injury, contamination or other liability from the use, storage, importation, handling or disposal of hazardous materials. If our or our suppliers' operations result in the contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and fines, and any liability could significantly exceed our insurance coverage and have a material adverse effect on our business, financial condition, results of operations and prospects. We maintain insurance for certain environmental risks, subject to substantial deductibles; however, we cannot assure you we can continue to maintain this insurance in the future at an acceptable cost, or at all. Future changes to environmental and health and safety laws could cause us to incur additional expenses or restrict our operations.

We are subject to anti-bribery, anti-corruption and anti-money laundering laws, including the U.S. Foreign Corrupt Practices Act, and violations of these laws could result in substantial penalties and prosecution

We are exposed to trade and economic sanctions and other restrictions imposed by the United States and other governments and organizations. The U.S. Departments of Justice, Commerce, State and Treasury and other federal agencies and authorities have a broad range of civil and criminal penalties they may seek to impose against corporations and individuals for violations of economic sanctions laws, export control laws, and other federal statutes and regulations, including sanctions administered by the Office of Foreign Assets Control and other U.S. governmental agencies. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products under the laws of the United States or other countries, could harm our ability to engage in international trade and adversely affect our revenue. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons or technologies targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers or to conduct business with foreign parties.

The FCPA, the UK Bribery Act of 2010 (the "Bribery Act"), and similar laws around the world generally prohibit U.S. companies and their employees and intermediaries from offering, promising, authorizing or making improper payments to foreign government officials for the purpose of obtaining or retaining business or gaining any advantage. We face significant risks if we, which includes our third party business partners and intermediaries, fail to comply with the FCPA or other anti-corruption and anti-bribery laws. In addition, the Bribery Act prohibits both domestic and international bribery, as well as bribery across both private and public sectors. An organization that "fails to prevent bribery" by anyone associated with the organization can be charged under the Bribery Act unless the organization can establish the defense of having implemented "adequate procedures" to prevent bribery. We have implemented policies and procedures to help ensure compliance with these laws, though such compliance measures ultimately may not be effective in prohibiting our employees, contractors, business partners, intermediaries or agents from violating or circumventing our policies and/or the law.

Under these laws and regulations, as well as other anti-corruption laws, anti-money laundering laws, export control laws, customs laws, sanctions laws and other laws governing our operations, various government agencies may require export licenses, may seek to impose modifications to business practices, including cessation of business activities in sanctioned countries or with sanctioned persons or entities and modifications to compliance programs, which may increase compliance costs, and may subject us to fines, penalties and other sanctions. An actual or alleged violation of these laws or regulations would negatively affect our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

We may not effectively be able to protect or enforce our intellectual property, which could have a material adverse effect on our business, financial condition, results of operations and prospects

The medical innovation market in which we participate is largely technology driven. Physicians historically have moved quickly to new products and new technologies. As a result, intellectual property rights, particularly patents and trade secrets, play a significant role in product development and differentiation. Patents enable us to stop unauthorized third parties from making, using, selling, offering for sale or importing products that are covered under valid and enforceable patents. Trade secrets enable us to protect information that we do not wish to divulge to the public. Trademarks also play a role in product differentiation. If we are unable to adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies or the goodwill we have acquired in the marketplace and erode or negate any competitive advantage we may have, which could ultimately harm our business and ability to achieve profitability. In order to protect our intellectual property, we may be involved in intellectual property litigation, which is inherently complex, expensive and unpredictable.

We hold patents and pending patent applications. Our patents cover inventions, which include features of our technologies or products. However, our competitors may seek to produce products that include our technologies that are not subject to patent protection, which may negatively affect our business.

The patents we own may not be sufficiently broad to protect our technology or to give us any competitive advantage. We are unable to provide any assurances that any of our patents, or patents to which we have rights through licensing agreements, have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our technology or products, any additional features we develop with respect to our technology or products, or any new technology or products that we seek to develop in the future. Our patents could be challenged as invalid or unenforceable, or circumvented by competitors. Medical device patents involve complex legal, scientific and factual questions, and therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Any patents for which we have applied may not be granted. Third parties own numerous U.S. and foreign issued patents and pending patent applications in the fields in which we have developed our technology or manufacture and sell our products. Third party-owned patents can be an obstacle to our ability to obtain patent protection for our technology.

Because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our products. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013 (the date when United States patent law changed from granting rights to the first-to-invent to the first-to-file), an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office (the “USPTO”), to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. We cannot be certain that we are the first to invent the inventions covered by pending patent applications entitled to a priority date before March 16, 2013, and, if we are not, we may be subject to priority disputes.

We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim, and we may be subject to a third-party pre-issuance submission of prior art to the USPTO. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim through a post-issuance proceeding or in litigation. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable, or that even if found valid and enforceable, a competitor’s technology or product would be found by a court to infringe our patents.

We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our products, but our competitors may obtain issued claims, including in patents we considered to be unrelated, which block our efforts or may potentially result in our technology or products or our activities infringing such claims. The possibility exists that others will develop technology or products which have the same effect as our technology or products on an independent basis which do not infringe our patents or other intellectual property rights or will design around the claims of patents that we have had issued that cover our technology or products.

Challenges raised in patent infringement litigation may cause determinations that our patents or licensed patents are invalid, unenforceable, or otherwise subject to limitations. In such events, third parties may use the discoveries or technologies without paying damages, licensing fees or royalties to us, which could significantly diminish the value of our intellectual property. We could also be adversely affected if our licensors terminate licenses granted to us to use their patented technology. Thus, any patents that we may own, or to which we have rights through licensing agreements, may not provide sufficient protection against competitors. Furthermore, an adverse decision in a judicial or administrative proceeding can result in a third party receiving the patent right sought by us, which, in turn, could affect our ability to commercialize our technology or products.

We hold trademark applications or registrations relating to our products. Our trademarks may also be challenged as invalid or not distinctive by competitors or third parties. Registration of a trademark is not conclusive as to its validity or the right to use such trademark. Third parties own numerous U.S. and foreign trademark registrations and trademark applications in the fields in which we manufacture and sell our products.

We may be unable to enforce our intellectual property rights throughout the world

Filing, prosecuting and defending patents covering our products in all countries throughout the world would be prohibitively expensive, and the laws of some foreign countries do not protect our intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This could make it difficult for us to stop infringement of our foreign patents, if obtained, or the misappropriation of our other intellectual property rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Hence, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in those countries. Our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

Additionally, in the event that our trademarks are successfully challenged in the United States and in jurisdictions outside of the United States, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our intellectual property rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in the United States and in jurisdictions outside of the United States could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Further, we may not always detect infringement of our intellectual property rights, and defending our intellectual property rights, even if successfully detected, prosecuted, enjoined, or remedied, could result in the expenditure of significant financial and managerial resources. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we cannot protect and control unpatented trade secrets, know-how and other proprietary technology, we may suffer competitive harm

Besides patented intellectual property, we also rely on trade secrets, unpatented proprietary technology, confidential information and know-how to protect our technology and maintain our competitive position, particularly when patent protection is not appropriate or obtainable. These include, but may not be limited to, with respect to Virtue SAB and other product candidates our Focal Therapies

group intends to develop, the chemical and physical aspects of the polymers and excipients in our formulation and the process by which our formulation is mixed, purified, concentrated, diluted, stored, filled into vials, freeze dried, sterilized, inspected, labeled and packaged, as well as physical and engineering aspects of our catheter, detailed specifications of our porous balloon, and physical and engineering aspects of our dose unit, recon unit, and pre-filled syringe. With respect to BackBeat CNT, this may include, but may not be limited to, certain aspects of our proprietary algorithms. However, trade secrets and unpatented proprietary technology are difficult to protect. To protect proprietary technology and processes, we rely in part on confidentiality and intellectual property assignment agreements with our employees, consultants and others. These agreements may not prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property and may not provide an adequate remedy if unauthorized disclosure of confidential information or other breaches of the agreements occur. Others may independently discover or reverse engineer our trade secrets and proprietary information licensed to us or that we own in a manner that could prevent legal recourse by us. Enforcing a claim that a party illegally obtained and is using trade secrets licensed to us or that we own is difficult, expensive and time consuming, and the outcome is unpredictable. In the United States, trade secret violations are both a matter of federal law and state law, and the criteria for protection of trade secrets under state law can vary among different jurisdictions. Courts outside the United States may be less willing to protect trade secrets or unpatented proprietary technology. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets

We employ individuals who previously worked with other companies, including our competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. Litigation may be necessary to defend against these claims. If we fail in defending any such claims or settling those claims, in addition to paying monetary damages or a settlement payment, we may be subject to an injunction and lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be involved in litigation or other proceedings relating to patent, trade secret and other intellectual property rights, which could cause substantial costs and liability

There may be patents and patent applications owned by our competitors, which, if determined to be valid and enforceable, may be infringed by us. We do not always conduct independent reviews of patents issued to third parties. Holders of certain patents may contact us and request we enter into license agreements for the underlying technology and pay them royalties, which could be substantial. If we need to obtain a license to use any intellectual property, we may be unable to obtain these licenses on favorable terms or at all or we may be required to make substantial royalty or other payments to use this intellectual property. Litigation concerning patents, trade secret and proprietary rights is time-consuming, expensive and unpredictable, and could divert the attention of our management from our business operations. Patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived, so there may be applications of others now pending or recently revived patents of which we are unaware. Patent applications in the United States, Europe and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. These applications that later result in issued patents, or the revival of previously abandoned patents, may prevent, limit or otherwise interfere with our ability to develop and market our products. Third parties may assert claims that we are employing their proprietary technology without authorization, including claims from competitors or from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect.

As we continue to commercialize our technology and products in their current or updated forms, launch new technologies and products and enter new markets, we expect competitors may claim that one or more of our technology or products infringe their intellectual property rights as a strategy to impede our commercialization and entry into new markets. The large number of patent issuances, the rapid rate of new patent application filings, the complexities of the technologies involved, and the uncertainty of litigation may increase the risk to our business and result in business resources and management’s attention being diverted to patent litigation. An adverse ruling in a patent litigation could subject us to significant liability, require us to seek licenses, and restrict our

ability to commercialize our technology or manufacture and sell our products. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources.

Additionally, we may become party to adversarial proceedings regarding our or third-party patent portfolios. Such proceedings could include supplemental examination or contested post-grant proceedings such as post-grant review, reexamination, inter partes review, interference or derivation proceedings before the USPTO, and challenges in U.S. District Courts. Patents may be subjected to opposition, post-grant review or comparable proceedings lodged in various foreign, both national and regional, patent offices. The legal threshold for initiating litigation or contested proceedings may be low, so that even lawsuits or proceedings with a low probability of success might be initiated. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. We may also occasionally use these proceedings to challenge the patent rights of others. We cannot be certain that any particular challenge will be successful in limiting or eliminating the challenged patent rights of the third party.

An unfavorable outcome in abovementioned lawsuits and proceedings could require us to pay substantial damages, to lose our patent protection, to cease using the technology or to license rights, potentially at a substantial cost, from prevailing third parties. There is no guarantee that any prevailing party would offer us a license or that we could acquire any license on commercially acceptable terms. Even if we can obtain rights to a third-party's intellectual property, those rights may be non-exclusive, and therefore our competitors may obtain access to the same intellectual property. Ultimately, we may have to cease some of our business operations because of infringement claims, which could severely harm our business. To the extent we are found to be infringing on the intellectual property rights of others, we may not develop or otherwise obtain alternative technology. If we need to redesign our products to avoid third-party intellectual property rights, we may suffer significant regulatory delays associated with conducting additional studies or submitting technical, manufacturing or other information related to any redesigned product and, ultimately, in obtaining regulatory approval. Further, any such redesigns may result in less effective or less commercially desirable products or both.

Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. Intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays, or prohibit us from manufacturing, importing, marketing or otherwise commercializing our products and technology. In addition, if the breadth or strength of protection provided by the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology or products. In addition, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our Common Stock could be adversely affected.

Lastly, we may need to indemnify our customers, licensees, commercialization partners, and distributors with respect to infringement by our technology or products of the intellectual property rights of third parties. Third parties may assert infringement claims against our customers, licensees, commercialization partners, or distributors based on our technology or products. These claims may require us to initiate or defend protracted and costly litigation on behalf of our customers, licensees, commercialization partners, or distributors, regardless of the merits of these claims. If any of these claims succeed or settle, we may be forced to pay damages or settlement payments on behalf of our customers, licensees, commercialization partners, or distributors or may be required to obtain licenses for the technology or products they use. If we cannot obtain all necessary licenses on commercially reasonable terms, our customers, licensees, commercialization partners, or distributors may be forced to stop using or selling our products or technology.

Patents covering our technology or products could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or interference proceedings or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights if patent rights are awarded to third

parties instead of to us. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications. Such challenges may result in loss of patent rights, in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology or products. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could have a material adverse effect on our business, financial condition and results of operations.

In addition, if we initiate legal proceedings against a third party to enforce a patent we own covering the third party's competing products, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise claims challenging the validity or enforceability of our patents before administrative bodies in the United States or abroad, even outside the context of litigation, including through re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (*e.g.*, opposition proceedings). Such proceedings could result in the revocation of, cancellation of or amendment to our patents in such a way that they no longer cover our products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product(s). Such a loss of patent protection would have a material adverse effect on our business, financial condition and results of operations.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements

Obtaining and maintaining our patent protection depends on compliance with various procedural measures, document submissions, fee payments and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in the abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition and results of operations.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act"), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a

period of time after filing or until issuance, we cannot be certain that we were the first to file any patent application related to our products or invent any of the inventions claimed in our patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Future actions by the U.S. Congress, the federal courts and the USPTO could cause the laws and regulations governing patents to change in unpredictable ways. Any of the foregoing could have a material adverse effect on our business, financial condition and results of operations.

We may be subject to claims challenging the ownership or inventorship of our patents and other intellectual property and, if unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, or to cease the development, manufacture and commercialization of one or more of our products

We may be subject to claims that current or former employees, collaborators or other third parties have an interest in our patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our products. Litigation may be necessary to defend against these and other claims challenging inventorship of our patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our products. If we were to jointly own such intellectual property with other owners, other owners may be able to license their rights to other third parties, including our competitors. We also may be required to obtain and maintain licenses from third parties, including parties involved in any such disputes. Such licenses may not be available on commercially reasonable terms, or at all, or may be non-exclusive. If we are in breach of any license agreements granted to us, such licenses may terminate. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture and commercialization of one or more of our products.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our products, when the terms of all patents covering a product expire, our business may become subject to competition from products identical or similar to ours which can be sold without infringing our patents. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may be unable to acquire patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation

In the United States, a patent that covers a medical device approved by the FDA may be eligible for a term extension designed to restore the period of the patent term that is lost during the pre-market regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our products, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Act”), which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the EU, our product candidates may be

eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

We may need to obtain intellectual property rights from third parties, and may not be successful in obtaining necessary rights to develop any future product through acquisitions and in-licenses

We may find it necessary or prudent to obtain licenses from third-party intellectual property holders to advance our research or to allow commercialization of our products, and we cannot provide any assurances that third-party intellectual property rights do not exist which might be enforced against our products in the absence of such a license. In addition, with respect to any patents we may in the future co-own with third parties, we may wish to acquire exclusive licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any intellectual property rights from third parties that we identify as necessary for planned or future products. The licensing or acquisition of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property licenses we have, we may have to abandon development of the relevant products, which could have a material adverse effect on our business, financial condition and results of operations.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected

Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be violating or infringing other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners and customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement or dilution claims brought by owners of other trademarks. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, domain names or other similar intellectual property may be ineffective, could result in substantial costs and diversion of resources and could adversely affect our business, financial condition and results of operations.

Risks Related to Ownership of Our Common Stock

Stockholder litigation and regulatory inquiries and investigations are expensive and could harm our business, financial condition and operating results and could divert management attention

In the past, securities class action litigation and/or stockholder derivative litigation and inquiries or investigations by regulatory authorities have often followed significant business transactions, such as the sale of a company or announcement of any other strategic transaction, such as the Business Combination. Any stockholder litigation and/or regulatory investigations against us, whether or not resolved favorably, could result in substantial costs and divert management's attention from other business concerns, which could adversely affect our business and cash resources.

Anti-takeover provisions contained in our Charter and our Bylaws and under Delaware law could impair a takeover attempt

Certain provisions of Delaware law, as well as provisions in our certificate of incorporation ("Charter") and our bylaws ("Bylaws"), may discourage unsolicited takeover proposals that stockholders may consider to be in their best interests. These

provisions may make it more difficult to remove management and may discourage transactions that otherwise could involve payment of a premium over prevailing market prices for our securities. Among other things, these provisions:

- allow our Board to authorize the issuance of undesignated preferred stock, the terms of which may be established and the shares of which may be issued without stockholder approval, and which may include supermajority voting, special approval, dividend, or other rights or preferences superior to the rights of other stockholders;
- provide for a classified board of directors with staggered three-year terms;
- provide that directors may only be removed for cause, and only by the affirmative vote of shares representing a majority of the shares entitled to vote at an election of directors;
- prohibit stockholder action by written consent;
- provide that special meetings may only be called by the Chairperson of the Board, the Chief Executive Officer or a majority of the directors;
- provide that we may indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law;
- provide that any adoption, amendment or repeal of any provision of the bylaws by our stockholders will require the affirmative vote of the holders of at least $66^{2}/_{3}$% of the voting power of all of the then-outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single class; and
- establish advance notice requirements for nominations for elections to the Board and for proposing matters that can be acted upon by stockholders at stockholder meetings.

Our charter provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forums for certain disputes between us and our stockholders, which could make our securities less attractive and impose legal costs on us if such limitations are challenged

Our charter provides that, unless we otherwise consent in writing, the Court of Chancery of the State of Delaware (or, in the event that the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, another state or federal court located within the State of Delaware) is, to the fullest extent permitted by law, the sole and exclusive forum for any:

- derivative action or proceeding brought on our behalf,
- action, suit or proceeding asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or stockholders to us or to our stockholders,
- action, suit or proceeding arising pursuant to any provision of the Delaware General Corporation Law (the “DGCL”), our charter or our bylaws, and
- action, suit or proceeding asserting a claim against us governed by the internal affairs doctrine.

This exclusive forum provision would not apply to suits brought to enforce a duty or liability vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, such as those created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction, or the Securities Act. In addition, to prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our charter provides that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. However, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, both state and federal courts have jurisdiction to entertain such claims. As noted above, our charter provides that the federal district courts of the

United States will be the exclusive forum for the resolution of any complaint asserting a cause of action under the Securities Act. Due to the concurrent jurisdiction for federal and state courts created by Section 22 of the Securities Act over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder, there is uncertainty as to whether a court would enforce the exclusive form provision. Our charter further provides that any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and to have consented to these provisions. Investors also cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

These exclusive forum provisions may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees and this limitation may make our securities less attractive to investors. Further, while the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring such a claim arising under the Securities Act against us or our directors, officers, or other employees in a venue other than in the federal district courts of the United States. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our charter. This may require significant additional costs associated with resolving such action in other jurisdictions and we cannot assure you that the provisions will be enforced by a court in those other jurisdictions. If a court were to find either exclusive-forum provision in our charter to be inapplicable or unenforceable in an action, it may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could harm our business.

The price of our securities may be volatile

Fluctuations in the price of our securities could contribute to the loss of all or part of your investment. The trading price of our securities has experienced volatility since the closing of the Business Combination. For example, from the closing of the Business Combination through October 6, 2023, the closing price of our Common Stock on the Nasdaq Global Market ranged from a high of $22.18 to a low of $5.08. The price of our Common Stock may continue to experience volatility in the future and is subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of such factors, including the factors listed below, could have a material adverse effect on your investment in our securities and our securities may trade at prices significantly below the price you paid. In such circumstances, the trading price of our securities may not recover and may experience a further decline.

Factors affecting the trading price of our securities may include:

- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- changes in the market’s expectations about our operating results;
- the inability to maintain our listing on Nasdaq;
- our operating results failing to meet the expectation of securities analysts or investors in a particular period;
- changes in financial estimates and recommendations by securities analysts concerning us or the market in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- our ability to develop product candidates;
- changes in laws and regulations affecting our business;
- litigation involving us;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of our securities available for public sale;

- any major change in our Board or management;
- sales of our securities by directors, executive officers or significant stockholders, or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

Broad market and industry factors may materially harm the market price of our securities irrespective of our operating performance. The stock market in general and Nasdaq in particular have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of our securities, may not be predictable. A loss of investor confidence in the market for medical device company stocks or the stocks of other companies which investors perceive to be similar to us could depress our stock price regardless of our business, prospects, financial conditions or results of operations. A decline in the market price of our securities also could adversely affect our ability to issue additional securities and our ability to obtain additional financing in the future.

Moreover, in the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

Our ability to timely raise capital in the future may be limited, or may be unavailable on acceptable terms, if at all. The failure to raise capital when needed could harm our business, operating results and financial condition. Debt or equity issued to raise additional capital may reduce the value of our Common Stock

We cannot be certain when or if our operations will generate sufficient cash to fund our ongoing operations or the growth of our business. We intend to make investments to support our current business and may require additional funds to respond to business challenges. Additional financing may not be available on favorable terms, if at all. If adequate funds are not available on acceptable terms, we may be unable to invest in our future growth opportunities, which could harm our business, operating results and financial condition. If we incur debt, the debt holders could have rights senior to holders of our Common Stock to make claims on our assets. The terms of any debt could restrict our operations, including our ability to pay dividends on our Common Stock. If we issue additional equity securities in the future, our stockholders will experience dilution, and the new equity securities could have rights senior to those of our Common Stock. Because the decision to issue securities in the future will depend on numerous considerations, including factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future issuances of debt or equity securities. As a result, stockholders will bear the risk of future issuances of debt or equity securities reducing the value of their common stock and diluting their interest.

The future sales, or the perception of future sales, of shares by existing stockholders and future exercise of registration rights may adversely affect the market price of our Common Stock

Sales of a substantial number of shares of our Common Stock in the public market could occur at any time. If our existing stockholders sell substantial amounts of Common Stock in the public market, or the market perceives that they intend to do so, the market price of our Common Stock could decline.

The holders of an aggregate of 21,812,857 shares of Common Stock (including 1,325,000 shares underlying warrants) are entitled to registration rights under the Amended and Restated Registration Rights Agreement and Lock-Up Agreement, dated as of January 26, 2023 (the “Amended and Restated Registration Rights Agreement”) entered into in connection with the closing of the Business Combination, and the registration of which this prospectus forms a part is registering the resale those outstanding shares of Common Stock as well as the issuance of shares of Common Stock underlying warrants. In certain circumstances, holders of these securities can demand that we conduct an underwritten offering of their securities or facilitate block trades of their securities. In addition, the holders have certain “piggy-back” registration rights with respect to registration statements we file. We will bear the expenses incurred in connection with the filing of any such registration statements. The presence of these additional shares trading in the public market may have an adverse effect on the market price of our securities.

Many of our existing stockholders are currently subject to lock-up provisions that restrict their ability to transfer certain of their shares of our Common Stock or any security convertible into or exercisable or exchange for our Common Stock until between 180 days after the time that the Merger became effective and one year after the closing of the Business Combination, subject to certain exceptions. As the restrictions on resale end, the market price of shares of our Common Stock could drop significantly if the holders of these shares of Common Stock sell them or are perceived by the market as intending to sell them. These factors could also make it more difficult for us to raise additional funds through future offerings of our shares of Common Stock or other securities.

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our Common Stock

If we fail to satisfy Nasdaq's continued listing requirements, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our Common Stock. Such a delisting would likely have a negative effect on the price of our Common Stock and would impair a stockholder's ability to sell or purchase our Common Stock when a stockholder wishes to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our Common Stock to become listed again, stabilize the market price or improve the liquidity of our Common Stock, prevent our Common Stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

If securities or industry analysts do not publish or cease publishing research or reports about us, our business, or our market, or if they change their recommendations regarding our securities adversely, the price and trading volume of our securities could decline

The trading market for our securities will be influenced by the research and reports that industry or securities analysts may publish about us, our business, our market, or our competitors. If any of the analysts who cover us change their recommendation regarding our Common Stock adversely, or provide more favorable relative recommendations about our competitors, the price of our securities would likely decline. If any analyst who covers or may cover us were to cease coverage or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

Because we do not anticipate paying any cash dividends in the foreseeable future, capital appreciation, if any, would be your sole source of gain

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any future determination to pay dividends will be made at the discretion of our Board, subject to applicable laws. It will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual, legal, tax and regulatory restrictions, general business conditions, and other factors that our Board may deem relevant. In addition, the ability to pay cash dividends may be restricted by the terms of debt financing arrangements, as any future debt financing arrangement likely will contain terms restricting or limiting the amount of dividends that may be declared or paid on our securities. As a result, capital appreciation, if any, of our securities would be your sole source of gain on an investment in such securities for the foreseeable future.

It may be more difficult to compare our performance to that of other public companies and our securities may be less attractive to investors if we take advantage of exemptions from disclosure requirements that are available to an "emerging growth company"

We qualify as an "emerging growth company" as defined in Section 2(a)(19) of the Securities Act, as modified by the JOBS Act. As such, we are eligible for certain exemptions available to emerging growth companies from various reporting requirements applicable to other public companies that are not emerging growth companies. We intend to take advantage of those exemptions for as long as we continue to be an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which the market value of our Common Stock that is held by non-affiliates exceeds $700 million as of June 30 of that fiscal year, (ii) the last day of the fiscal year in which we have total annual gross revenue of $1.235 billion or more during such fiscal year (as indexed for inflation), (iii) the date on which we have issued more than $1 billion in non-convertible debt in the prior three-year period or (iv) the last day of the fiscal year following the fifth anniversary of the date of the first sale of shares by our predecessor in its initial public offering.

The exemptions available to emerging growth companies include: (a) exemption from the auditor attestation requirements with respect to internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act, (b) exemptions from say-on-pay, say-on-frequency and say-on-golden parachute voting requirements and (c) reduced disclosure obligations regarding executive compensation in its periodic reports and proxy statements. In addition, Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the exemption from complying with new or revised accounting standards provided in Section 7(a)(2)(B) of the Securities Act as long as we are an emerging growth company. An emerging growth company can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected not to opt out of such extended transition period and, therefore, we may not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. This may make it more difficult to compare our performance to that of other public companies which could make our securities less attractive, which may result in a less active and more volatile trading market for our securities.

We may not be able to timely and effectively implement controls and procedures required by Section 404 of the Sarbanes-Oxley Act, which could have a material adverse effect on our business

Pursuant to Section 404 of the Sarbanes-Oxley Act, and in light of SEC guidance, management is required to report our assessment of internal control over financial reporting beginning with the fiscal year ending December 31, 2023, and, if and when we become an accelerated filer or large accelerated filer who is not eligible to be a smaller reporting company and has annual revenues of at least $100.0 million (and cease to be an emerging growth company), an attestation of the independent registered public accounting firm will also be required. The rules governing the standards that must be met for management to assess internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the Sarbanes-Oxley Act, the requirements of being a reporting company under the Exchange Act and any complex accounting rules in the future, we may need to upgrade our legacy information technology systems, implement additional financial and management controls, reporting systems and procedures, and hire additional accounting and finance staff or retain additional outside consultants.

If we are unable to implement the additional requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner or with adequate compliance, we may not be able to assess whether our internal control over financial reporting is effective, which may subject us to adverse regulatory consequences and could harm investor confidence and lead to a decrease in the market price of our securities. We could become subject to investigations by Nasdaq, the SEC or other regulatory authorities, which could require additional financial and management resources.

We will incur significant increased expenses and administrative burdens as a public company, which could negatively impact our business, financial condition and results of operations

We face increased legal, accounting, administrative and other costs and expenses as a public company. These increased costs require us to divert a significant amount of money and management attention that could otherwise be used to expand the business and achieve strategic objectives.

There are significant financial costs and expenses for complying with the Sarbanes-Oxley Act, including the requirements of Section 404, as well as rules and regulations of the SEC, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the rules and regulations thereunder, rules and regulations of the Public Company Accounting Oversight Board (“PCAOB”) and the securities exchanges. Compliance with public company requirements increase costs and make regulated activities more time-consuming. Advocacy efforts by stockholders and third parties may also prompt additional changes in governance and reporting requirements, which could further increase costs and administrative burdens. In order to comply with these requirements, we carry out activities that Legacy Orchestra had not done previously. For example, we will create and adopt new internal controls and disclosure controls and procedures, all of which will increase expenses and administrative burdens. In addition, we have new expenses associated with SEC reporting requirements.

Furthermore, if any issues in complying with those requirements are identified (for example, if the auditors identify a material weakness or significant deficiency in the internal control over financial reporting), we could incur further additional costs to remediate those issues. It may also be more expensive to obtain director and officer liability insurance. Risks associated with our status as a public company may make it more difficult to attract and retain qualified persons to serve on our Board or as executive officers. The additional reporting and other obligations imposed by these rules and regulations increase legal and financial compliance costs and the costs of related legal, accounting and administrative activities. These increased costs require us to divert a significant amount of money that could otherwise be used to expand the business and achieve strategic objectives.

Changes in laws or regulations, or a failure to comply with any laws and regulations, may adversely affect our business, investments and results of operations

We are subject to laws and regulations enacted by national, regional and local governments. In particular, we are required to comply with certain SEC, Nasdaq and other legal requirements. Compliance with, and monitoring of, applicable laws and regulations may be difficult, time consuming and costly. Those laws and regulations and their interpretation and application may also change from time to time and those changes could have a material adverse effect on our business, investments and results of operations. In addition, a failure to comply with applicable laws or regulations, as interpreted and applied, could have a material adverse effect on our business and results of operations.

MARKET AND INDUSTRY DATA

Certain information contained in this prospectus relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this prospectus, we have not independently verified the market and industry data contained in this prospectus or the underlying assumptions relied on therein. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source. Notwithstanding the foregoing, we are liable for the information provided in this prospectus. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section of this prospectus titled "*Risk Factors.*" These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

USE OF PROCEEDS

We will receive no proceeds from the sale of the Resale Shares or the Warrants by the Selling Securityholders. The Selling Securityholders will pay any underwriting discounts, selling commissions or transfer taxes incurred in disposing of the Resale Shares and the expenses of any attorney or other advisor they decide to employ, except that, pursuant to the Amended and Restated Registration Rights Agreement, in the context of an underwritten offering, the Company has agreed to pay the reasonable and documented fees and expenses of one legal counsel to the Selling Securityholders. We will bear all other costs, fees and expenses incurred in effecting the registration of the Resale Shares and the Warrants covered by this prospectus. These may include, without limitation, all registration, filing, stock exchange fees, printing expenses, all fees and expenses of complying with applicable securities laws and the fees and disbursements of our counsel and of our independent accountants and reasonable fees.

We will receive up to an aggregate of approximately $21.2 million from the exercise of the Warrants, assuming the exercise in full of all of the Warrants for cash, but will not receive any proceeds from the sale of the shares of our Common Stock issuable upon such exercise. We expect to use the net proceeds from the exercise of the Warrants for cash, if any, for working capital and general corporate purposes, which may include research and development expenditures, regulatory affairs expenditures, clinical trial expenditures, capital expenditures, acquisitions of new technologies and investments, business combinations and the repayment, refinancing, redemption or repurchase of indebtedness or capital stock. However, we have not designated any specific uses and have no current agreement with respect to any acquisition or strategic transaction. As of the date of this prospectus, we cannot specify with certainty all of the particular uses, and the respective amounts we may allocate to those uses, for any proceeds we may receive from the exercise of the Warrants. Accordingly, we will retain broad discretion over the use of these proceeds. Pending our use of the proceeds as described above, we intend to invest such proceeds in interest-bearing instruments. There is no assurance that the holders of the Warrants will elect to exercise any or all of such Warrants. To the extent that the Warrants are exercised on a “cashless basis,” the amount of cash we would receive from the exercise of the Warrants will decrease.

DETERMINATION OF OFFERING PRICE

The offering price of the shares of Common Stock underlying the HSAC2 Warrants and Officer and Director Warrants offered hereby is determined by reference to the exercise price of the HSAC2 Warrants Officer and Director Warrants of $11.50 per share.

The offering price of the shares of Common Stock underlying the Orchestra Warrants offered hereby is determined by reference to the exercise price of the Orchestra Warrants, as follows:

- Warrants to purchase an aggregate of 87,916 shares of Common Stock at an exercise price of $10.22 per share;
- Warrants to purchase an aggregate of 319,925 shares of Common Stock at an exercise price of $10.22 per share;
- Warrants to purchase an aggregate of 100,000 shares of Common Stock at an exercise price of $4.06 per share.

We cannot currently determine the price or prices at which shares of our Common Stock or Warrants may be sold by the Selling Securityholders under this prospectus.

MARKET INFORMATION FOR SECURITIES AND DIVIDEND POLICY

Market Information

Our Common Stock is currently listed on the Nasdaq Global Market under the symbol "OBIO."

Prior to the consummation of the Business Combination, HSAC2's ordinary shares were listed on the Nasdaq Capital Market under the symbol "HSAQ."

As of October 6, 2023, there were 511 holders of record of our Common Stock, which amount does not include participants of The Depository Trust Company or beneficial owners holding shares through nominee names.

Dividend Policy

We have not paid any cash dividends on our Common Stock to date. We anticipate that we will retain all of our future earnings, if any, for the development, operation and expansion of our business and we do not anticipate declaring or paying any cash dividends for the foreseeable future. Any future determination to pay dividends will be made at the discretion of our Board, subject to applicable laws. Such determination will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual, legal, tax and regulatory restrictions, general business conditions, and other factors that our Board may deem relevant. Should we decide in the future to do so, as a holding company, our ability to pay dividends on our capital stock and meet other obligations depends upon the receipt of dividends or other payments from our operating subsidiaries, including Legacy Orchestra. In addition, the ability to pay cash dividends may be restricted by the terms of debt financing arrangements, as any future debt financing arrangement likely will contain terms restricting or limiting the amount of dividends that may be declared or paid on our securities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

For purposes of this "Management's Discussion and Analysis of Financial Condition and Results of Operations" section, unless otherwise indicated or the context otherwise requires, references to "Orchestra," "Orchestra's, "the Company," "we," "its," and "our" refer to Legacy Orchestra and its consolidated subsidiaries prior to the Business Combination and to Orchestra BioMed Holdings, Inc. and its consolidated subsidiaries after the Business Combination. All references to years, unless otherwise noted, refer to the Company's fiscal years, which end on December 31.

The following discussion should be read in conjunction with the audited and unaudited condensed consolidated financial statements, including the notes thereto, included elsewhere in this prospectus. In addition to historical financial information, this discussion contains forward-looking statements based upon our current expectations that involve risks and uncertainties. Our actual results could differ materially from such forward-looking statements as a result of various factors, including those set forth under "Risk Factors" and elsewhere in this prospectus.

Closing of Business Combination

Prior to January 26, 2023, the Company was a special purpose acquisition company formed for the purpose of entering into a merger, amalgamation, share exchange, asset acquisition, share purchase, reorganization or similar business combination with one or more businesses or entities. On January 26, 2023, we consummated the Business Combination contemplated by the Merger Agreement. Pursuant to the Merger Agreement, (i) HSAC2 deregistered in the Cayman Islands in accordance with the Companies Act (2022 Revision) (As Revised) of the Cayman Islands and completed the Domestication and (ii) the Merger was completed. As part of the Domestication, we changed our name from "Health Sciences Acquisitions Corporation 2" to "Orchestra BioMed Holdings, Inc." On January 27, 2023, the Common Stock began trading on the Nasdaq Global Market under the symbol "OBIO." For additional information, see Note 3 to our unaudited condensed consolidated financial statements as of and for the three and six months ended June 30, 2023 (our "Condensed Consolidated Financial Statements").

Reverse Recapitalization

The Business Combination is accounted for as a reverse recapitalization (the "Reverse Recapitalization") in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Under this method of accounting, HSAC2 is treated as the "acquired" company and Legacy Orchestra is treated as the acquirer for financial reporting purposes. As a result, the consolidated assets, liabilities and results of operations prior to the Reverse Recapitalization are those of Legacy Orchestra. Additionally, the shares and corresponding capital amounts and losses per share, prior to the Business Combination, have been retroactively restated based on the exchange ratio established in the Merger Agreement ("Exchange Ratio").

Overview

We are a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. Our partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products we develop. We are led by a highly accomplished, multidisciplinary management team and a board of directors with extensive experience in all phases of therapeutic device development. Our business was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by our founding team. Our flagship product candidates are BackBeat CNT for the treatment of HTN, the leading risk factor for death worldwide, and Virtue SAB for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. We have a strategic collaboration with Medtronic for the development and commercialization of BackBeat CNT for the treatment of hypertension in patients indicated for a pacemaker. We have a strategic collaboration with Terumo for the development and commercialization of Virtue SAB for the treatment of coronary and peripheral artery disease.

Since Legacy Orchestra's inception, we have devoted the substantial majority of our resources to performing research and development and clinical activities in support of our product development and collaboration efforts. We have funded our operations primarily through the issuance of convertible preferred stock and proceeds from the Business Combination, as well as through proceeds from our distribution agreement (the "Terumo Agreement") with Terumo, borrowings under debt arrangements and, to a lesser extent, from product revenue from our subsidiary, FreeHold. We have raised a cumulative $166.8 million in gross proceeds through the issuance of convertible preferred stock, $70.0 million in gross proceeds from the Business Combination, and have

received $30.0 million from the Terumo Agreement through June 30, 2023. We have incurred net losses each year since inception. Our net losses were $12.0 million and $7.8 million for the three months ended June 30, 2023 and 2022, respectively, and $23.0 million and $13.6 million for the six months ended June 30, 2023 and 2022, respectively. We expect to continue to incur significant losses for the foreseeable future. As of June 30, 2023, we had an accumulated deficit of $222.7 million.

Legacy Orchestra was incorporated in Delaware in 2017 and completed a recapitalization and mergers with Caliber Therapeutics, Inc., a Delaware corporation that has, among other things, the rights to the Virtue SAB product candidate and BackBeat Medical, Inc., a Delaware Corporation that has, among other things, the rights to the Backbeat CNT product candidate, in 2018. Legacy Orchestra completed the conversions of Caliber Therapeutics, Inc. to Caliber Therapeutics, LLC, a Delaware limited liability company, and BackBeat Medical, Inc. to BackBeat Medical, LLC, a Delaware limited liability company, in 2019.

Recent Developments

On September 19, 2023, we announced that the FDA granted us IDE approval to initiate our planned BACKBEAT pivotal study of BackBeat CNT, also known as AVIM therapy, to treat hypertension in patients indicated for a pacemaker. We currently expect to initiate enrollment of the BACKBEAT pivotal study before the end of 2023 following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals.

On August 8, 2023, we announced that the FDA granted us investigational device exemption approval with conditions to initiate our planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary ISR. The conditional approval permits us to initiate enrollment of the Virtue ISR-US pivotal study following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals. We are also required to submit additional information to the FDA.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to the Terumo Agreement that could serve to restructure milestone payments as well as make other potential material modifications to the Terumo Agreement. Until we gain clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development efforts, and commercialization plans for Virtue SAB may continue to be adversely impacted.

On October 6, 2023, the Company repaid and terminated the 2022 Loan and Security Agreement. In connection with the repayment and termination, the Company repaid $10 million of principal and issued warrants to purchase 27,707 shares of Company Common Stock at an exercise price of $7.67 per share in lieu of a cash payment of approximately $212,500 due with respect to certain fees under the 2022 Loan and Security Agreement. The Company also paid approximately $849,000 of net interest, prepayment fees, and legal fees.

COVID-19 Impact and Business Update

Outbreaks of contagious disease, including COVID-19, or other adverse public health developments in the United States or worldwide could have a material adverse effect on our business, including our clinical trials and financial condition. While many of the direct impacts of the COVID-19 pandemic have eased, the longer-term macroeconomic effects on global supply chains, inflation, labor shortages and wage increases continue to impact many industries, including ours. Moreover, with the potential for new strains of existing viruses to emerge, or other pandemics or epidemics, governments and businesses may re-impose aggressive measures to help slow the spread of disease in the future. Long-term macroeconomic effects from a pandemic or epidemic, including from supply and labor shortages and workforce reductions in response to challenging economic conditions, may have an adverse impact on our business. In addition, COVID-19 caused, and any future pandemic or epidemic may cause, delays with respect to regulatory approvals or certifications for clinical studies, the initiation of clinical studies and the coordination of follow-up with respect to clinical studies, as well as delays in receiving supplies and third-party testing results from vendors.

We continue to actively monitor the impact of the COVID-19 pandemic on our development programs. To date, we experienced some impacts on our development programs due to the pandemic, including delays in receiving products and services from certain of our manufacturing and other key vendors as a direct or indirect result of the COVID-19 pandemic, including supply chain issues, and competition for manufacturing capacity from manufacturers of COVID-19 related therapeutics. We also experienced challenges related to recruiting, enrolling and treating patients in clinical studies due to patients' concern regarding exposure risk; patients and

clinical study staff being exposed to the virus that causes COVID-19 or contracting COVID-19; reduced staffing at clinical study sites due to the diversion of resources at clinical sites to address the effects of the pandemic; and travel restrictions and shutdowns impacting patients and clinical study staff. While many of these impacts have been resolved, we continue to monitor our clinical development and supply chain and contingency planning is ongoing with our partners to reduce the possibility and magnitude of interruptions to our development activities or the availability of necessary materials.

The full extent of the impact and effects of COVID-19, and any future pandemics or epidemics, will depend on future developments, including, among other factors, how rapidly variants develop, availability, acceptance and effectiveness of vaccines along with related travel advisories, quarantines and restrictions, the recovery time of the disrupted supply chains and industries, the impact of labor market interruptions, the impact of government interventions, and uncertainty with respect to the duration of the global economic slowdown. We continue to actively monitor the situation related to COVID-19 and any future pandemics or epidemics and may take further actions that alter our operations, including those that federal, state or local authorities may require, or that we determine are in the best interests of our clinical study subjects, employees and other third parties with whom we do business. While the direct impacts of the COVID-19 pandemic have eased, the extent to which the COVID-19 pandemic may affect our future business, operations and development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

Components of Our Results of Operations

Partnership Revenue

To date, our partnership revenues have related to the Terumo Agreement described below. In future periods, partnership revenues may also include revenues related to the Exclusive License and Collaboration Agreement, dated as of June 30, 2022, by and among, Legacy Orchestra, BackBeat Medical, LLC and Medtronic (the “Medtronic Agreement”).

Legacy Orchestra entered into the Terumo Agreement in June 2019, and has determined that the arrangement represents a contract with a customer and is therefore in scope of ASC 606, *Revenues from Contracts with Customers* (“ASC 606”). Under the Terumo Agreement, Legacy Orchestra received an upfront payment of $30.0 million in 2019 and an equity commitment of up to $5 million of which $2.5 million was invested in June 2019 as part of the Legacy Orchestra Series B-1 financing and $2.5 million was invested in June 2022 as part of the Legacy Orchestra Series D-2 financing (the “Series D-2 Financing”).

Under the Terumo Agreement, we were initially eligible for certain milestone payments in the amount of $65 million from Terumo upon completion of certain minimum enrollments in clinical studies, making certain filings and submissions, and obtaining certain regulatory approvals and certifications, and are also eligible to earn royalties on future sales by Terumo based on royalty rates ranging from 10-15%. Of these milestone payments, $35 million relate to achieving certain milestones by specified target achievement dates. As of the date of this prospectus, we have already passed the target achievement dates for two $5 million milestone payments, in each case, without achieving the related milestones. In addition, due to delays in our Virtue SAB program resulting from the COVID-19 pandemic, supply chain issues and unexpected regulatory delays and requirements, including increased testing and other activities related to chemistry, manufacturing, and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, that caused us to amend our original project plan, we are unlikely to be able to complete the remaining time-based milestones by the specified target achievement dates to earn the remaining $25 million in time-based milestone payments pursuant to the Terumo Agreement. Further, Terumo has the right to terminate the agreement, or certain of its obligations thereunder, if certain milestones are not achieved.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to the Terumo Agreement that could serve to restructure milestone payments as well as make other potential material modifications to the Terumo Agreement. Until we gain clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development, and commercialization plans for Virtue SAB may continue to be adversely impacted.

We recorded the $30.0 million upfront payment received in 2019 from Terumo within deferred revenue and are recognizing the upfront payment over time based on a proportional performance model based on the costs incurred to date relative to the total costs expected to be incurred through the completion of the development of the coronary ISR indication, for which we are primarily

responsible. We have recognized $12.2 million in cumulative partnership revenues from 2019 through June 30, 2023. There were no other proceeds received pursuant to the Terumo Agreement from 2019 through June 30, 2023.

In June 2022, Legacy Orchestra entered into the Medtronic Agreement for the development and commercialization of BackBeat CNT for the treatment of HTN in patients indicated for a cardiac pacemaker. We have determined that the arrangement is a collaboration within the scope of *ASC 808*, *Collaborative Arrangements* (“ASC 808”). In addition, we concluded that Medtronic, is a customer for a good or service that is a distinct unit of account, and therefore, the transactions in the Medtronic Agreement should be accounted for under ASC 606. Through June 30, 2023, there have been no amounts recognized as revenue under the Medtronic Agreement.

Product Revenue

Product revenues related to sales of FreeHold’s intracorporeal organ retractors and such revenues are recognized at a point-in-time upon the shipment of the product to the customer given payment terms are typically 30 days. FreeHold products are currently only sold in the United States.

Cost of Product Revenue and Gross Margin

Cost of product revenue consists primarily of costs of finished goods components for use in FreeHold’s products and assembled, warehoused and inventoried by a third-party vendor. We expect cost of finished goods product revenue to increase in absolute terms as our revenue grows.

Our gross margin has been and will continue to be affected by a variety of factors, including finished goods manufactured component parts and the cost to assemble and warehouse the FreeHold product finished goods inventory.

Research and Development Expenses

Research and development expenses consist of applicable personnel, consulting, materials and clinical study expenses. Research and development expenses include:

- Certain personnel-related expenses, including salaries, benefits, bonus, travel and stock-based compensation;
- Cost of clinical studies to support new products and product enhancements, including expenses for clinical research organizations and site payments;
- Product device materials and drug supply and manufacturing used for internal research and development and clinical activities;
- Allocated overhead including facilities and information technology expenses; and
- Cost of outside consultants who assist with device and drug development, regulatory affairs, clinical affairs and quality assurance.

Research and development costs are expensed as incurred. Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical studies. In the future, we expect research and development expenses to increase in absolute dollars as we continue to develop new products, enhance existing products and technologies, initiate clinical studies, manufacture drug supply for internal research and development and clinical trial supply and perform activities related to obtaining additional regulatory approvals. We do not track expenses by product candidate, unless tracking such expenses is required pursuant to the revenue recognition model for a collaborative arrangement.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist of personnel-related expenses, including salaries, benefits, bonus, travel and stock-based compensation. Other selling, general and administrative expenses include professional services fees, including legal, audit investor/press relations, non-income taxes, insurance costs, cost of outside consultants and employee recruiting and training costs. Moreover, we incur and expect to continue to incur additional expenses associated with operating as a public company, including legal, accounting, insurance, exchange listing and SEC compliance and investor relations. We expect quarterly selling, general and administrative expenses, excluding stock-based compensation expense, to continue to increase as a public company.

Interest Income (Expense), Net

Interest income reflects the income generated from marketable securities during the year. Interest expense is attributable to loan interest.

In June 2022, Legacy Orchestra entered into a loan and security agreement (the "2022 Loan and Security Agreement") with Avenue Venture Opportunities Fund, L.P. ("Avenue I") and Avenue Venture Opportunities Fund II, L.P. ("Avenue II," and, collectively with Avenue I, "Avenue"). As part of the 2022 Loan and Security Agreement, Legacy Orchestra paid off the balance of the 2019 Loan and Security Agreement (as defined below) with Silicon Valley Bank. The terms of the 2022 Loan and Security Agreement include a term loan of up to $20 million available in two tranches with the first tranche of $10 million that was drawn at closing in June of 2022, and a second tranche of $10 million available at closing of the Series D-2 Financing that was not drawn. Additionally, we may have access to a third tranche of $30 million subject to certain financing milestones. The term loan had a maturity date of June 1, 2026 and accrued interest at a floating per annum rate equal to the Wall Street Journal prime rate plus 6.45%. The rate in effect at June 30, 2023 was 14.7%. On October 6, 2023, the 2022 Loan and Security Agreement was repaid in full and terminated.Refer to Note 14 to our Condensed Consolidated Financial Statements.

In December 2019, Legacy Orchestra entered into a Loan and Security Agreement with Silicon Valley Bank for a term loan as described in Note 14 to our Condensed Consolidated Financial Statements (the "2019 Loan and Security Agreement"). The 2019 Loan and Security Agreement provided Legacy Orchestra with capital for development and general corporate purposes. On December 31, 2020, Legacy Orchestra borrowed $10 million under the 2019 Loan and Security Agreement.

Gain (Loss) on Fair Value Adjustment of Warrant Liability

Certain of Legacy Orchestra's outstanding warrants contained features that required the warrants to be accounted for as liabilities. The warrants were subject to re-measurement at each balance sheet date with gains and losses reported through Legacy Orchestra's condensed consolidated statements of operations and comprehensive loss as gain (loss) on fair value adjustment of warrant liability. Upon closing of the Business Combination, all liability classified warrants of Legacy Orchestra became equity classified on that date as they are now considered "fixed for fixed."

Gain (Loss) on Fair Value of Strategic Investments

The gain (loss) on fair value of strategic investments represents a change in the fair value of our investment in Motus GI Holdings, Inc. ("Motus GI"), a publicly-held company and related party, and preferred shares and convertible notes of Vivasure Medical Limited ("Vivasure"), a privately-held company and related party. The shares held of Motus GI represent equity securities with a readily determinable fair value and are required to be measured at fair value at each reporting period using readily determinable pricing available on a securities exchange, in accordance with the provisions of ASU 2016-01, *Recognition and Measurement of Financial Assets and Liabilities*. The investments in Vivasure do not have readily determinable fair values and are recorded at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for identical or similar investments of the same issuer.

Results of Operations

Comparison of the Six Months Ended June 30, 2023 and 2022

The following table presents our statement of operations data for the six months ended June 30, 2023 and 2022, and the dollar and percentage change between the two periods (in thousands):

	Six Months Ended June 30,			
	2023	2022	Change $	Change %
Revenue:				
Partnership revenue	$ 1,747	$ 945	$ 802	85%
Product revenue	332	322	10	3%
Total revenue	2,079	1,267	812	64%
Expenses:				
Cost of product revenues	98	102	(4)	(4)%
Research and development	16,753	8,503	8,250	97%
Selling, general and administrative	9,729	5,424	4,305	79%
Total expenses	26,580	14,029	12,551	89%
Loss from operations	(24,501)	(12,762)	(11,739)	(92)%
Other income (expense):				
Interest income (expense), net	1,826	(482)	2,308	479%
Loss on fair value adjustment of warrant liability	(294)	(1,160)	866	75%
Loss on debt extinguishment	—	(682)	682	100%
(Loss) gain on fair value of strategic investments	(17)	1,510	(1,527)	(101)%
Total other income (expense)	1,515	(814)	2,329	286%
Net loss	$ (22,986)	$ (13,576)	$ (9,410)	(69)%

Partnership Revenue

Partnership revenue increased by $802,000, or approximately 85%, to $1.7 million in the six months ended June 30, 2023 from $945,000 for the six months ended June 30, 2022. Partnership revenue relates to the recognition of the combined performance obligation for the license granted to Terumo and the ongoing research and development services over the estimated performance period for the Virtue SAB coronary ISR indication, using a proportional performance model, based on the costs incurred relative to the total estimated costs of the research and development services. As of each quarterly reporting date, we evaluate our estimates of the total costs expected to be incurred through the completion of the combined performance obligation and update our estimates as necessary.

For the six months ended June 30, 2023 and 2022, the expenses incurred related to the Terumo Agreement were approximately $8.3 million and $6.6 million, respectively. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 3% as of June 30, 2023 as compared to the estimates as of December 31, 2022, and increased by approximately 10% as of June 30, 2022, as compared to the estimates as of December 31, 2021.

While we believe we have estimated total costs associated with the Terumo Agreement through completion, these estimates encompass a broad range of expenses over a multi-year period and, as such, are subject to periodic changes as new information becomes available.

Product Revenue

Product revenue increased by $10,000, or approximately 3%, to $332,000 in the six months ended June 30, 2023 from $322,000 for the six months ended June 30, 2022.

Product revenue consisted of the sale of FreeHold Duo and Trio intracorporeal organ retractors and revenue is recognized when product is shipped to customers. The increase in product revenue was primarily due to a increase in the purchase volume of FreeHold Duo and Trio intracorporeal organ retractors. There were no changes to the per unit sale price in either period presented.

Cost of Product Revenue

Cost of product revenue decreased by $4,000, or approximately 4%, to $98,000 in the six months ended June 30, 2023 from $102,000 for the six months ended June 30, 2022. The decrease was primarily due to decreased production costs of FreeHold Duo and Trio intracorporeal organ retractors.

Research and Development Expenses

The following table summarizes our research and development expenses for the six months ended June 30, 2023 and 2022 (in thousands):

	Six Months Ended June 30,	
	2023	2022
Personnel and consulting costs	8,088	3,908
Non-clinical development costs	6,601	3,856
Clinical development costs	2,064	739
Total research and development expenses	$ 16,753	$ 8,503

Research and development expenses increased by $8.3 million, or approximately 97%, to $16.8 million for the six months ended June 30, 2023 from $8.5 million for the six months ended June 30, 2022. This is primarily due to an increase in support of ongoing work to advance BackBeat CNT and Virtue SAB into planned pivotal studies during 2023 and included an increase in personnel related expenses of $3.2 million due to increased headcount and associated expenses, along with increased stock-based compensation of $932,000, an increase of $2.7 million in research and development program costs, supplies, and testing, and an increase of $1.3 million in clinical development costs.

The total research and development expenses summarized above include $8.2 million for the six months ended June 30, 2023 and $6.3 million for the six months ended June 30, 2022 related to the Terumo Agreement. The increase of $1.9 million is due to increased expense activity related to the Terumo Agreement during the 2023 period.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $4.3 million, or approximately 79%, to $9.7 million for the six months ended June 30, 2023, from $5.4 million of expense for the six months ended June 30, 2022. The increase was primarily due to an increase in headcount which resulted in a $232,000 increase in salary and medical benefit costs, along with increased stock-based compensation of $2.0 million, and an increase of $1.3 million of accounting, finance, legal expenses, investor relations and public relations expenses incurred in connection with the overall growth of the business and in preparation for becoming and being a public company.

Interest Income (Expense), Net

Interest income (expense), net, increased by $2.3 million, or approximately 479%, to $1.8 million of income for the six months ended June 30, 2023, from $482,000 of expense for the six months ended June 30, 2022. The net interest income in the 2023 period consisted primarily of interest earned from marketable securities offset by monthly interest expense incurred resulting from the 2022 Loan and Security Agreement. The net interest expense in the 2022 period consisted primarily of interest expense incurred resulting from the December 31, 2020 drawdown of the $10.0 million tranche from the 2019 Loan and Security Agreement.

Loss on Fair Value Adjustment of Warrant Liability

The loss on fair value adjustment of warrant liability was a loss of $294,000 for the six months ended June 30, 2023, as compared to a loss of $1.2 million for the six months ended June 30, 2022. The change year over year is primarily a result of the change in the fair value of our outstanding warrants due to an increase in the fair value of the underlying Common Stock.

Loss on Debt Extinguishment

The loss on debt extinguishment was $682,000 for the six months ended June 30, 2022. The loss was due to recognition of unamortized debt discount as well as early termination payments related to the early termination and repayment of the 2019 Loan and Security Agreement in June 2022.

(Loss) Gain on Fair Value of Strategic Investments

The loss in fair value of strategic investments was $17,000 for the six months ended June 30, 2023, as compared to a gain of $1.5 million for the six months ended June 30, 2022. The amounts recognized for the six months ended June 30, 2023 related to the change in fair value in our common stock holdings of Motus GI. The amount recognized for the six months ended June 30, 2022, relates to a gain on our strategic investment in Vivasure of $1.9 million, partially offset by the change in fair value in our common stock holdings of Motus GI. The gain on our strategic investment in Vivasure was attributable to an observable price change for an identical investment due to a new third-party investment. Therefore, the investment was measured at fair value and a gain was recognized.

Comparison of the Three Months Ended June 30, 2023 and 2022

The following table presents our statement of operations data for the three months ended June 30, 2023 and 2022, and the dollar and percentage change between the two periods (in thousands):

	Three Months Ended June 30,			
	2023	2022	Change $	Change %
Revenue:				
Partnership revenue	$ 728	$ 229	$ 499	$ 218%
Product revenue	187	172	15	9%
Total revenue	915	401	514	128%
Expenses:				
Cost of product revenues	54	60	(6)	(10)%
Research and development	8,499	5,029	3,470	69%
Selling, general and administrative	5,318	2,946	2,372	81%
Total expenses	13,871	8,035	5,836	73%
Loss from operations	(12,956)	(7,634)	(5,322)	(70)%
Other income (expense):				
Interest income (expense), net	941	(246)	1,187	483%
Loss on fair value adjustment of warrant liability	—	(1,015)	1,015	100%
Loss on debt extinguishment	—	(682)	682	100%
(Loss) gain on fair value of strategic investments	(31)	1,730	(1,761)	(102)%
Total other income (expense)	910	(213)	1,123	527%
Net loss	$ (12,046)	$ (7,847)	$ (4,199)	$ (54)%

Partnership Revenue

Partnership revenue increased by $499,000, or approximately 218%, to $728,000 in the three months ended June 30, 2023 from $229,000 for the three months ended June 30, 2022. Partnership revenue relates to the recognition of the combined performance obligation for the license granted to Terumo and the ongoing research and development services over the estimated performance period for the Virtue SAB coronary ISR indication, using a proportional performance model, based on the costs incurred relative to the total estimated costs of the research and development services. As of each quarterly reporting date, we evaluate our estimates of the total costs expected to be incurred through the completion of the combined performance obligation and update our estimates as necessary.

For the three months ended June 30, 2023 and 2022, the expenses incurred related to the Terumo Agreement were approximately $4.5 million and $3.9 million, respectively. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 3% as of June 30, 2023 as compared to the estimates as of March 31, 2023, and increased by approximately 10% as of June 30, 2022, as compared to the estimates as of March 31, 2022.

While we believe we have estimated total costs associated with the Terumo Agreement through completion, these estimates encompass a broad range of expenses over a multi-year period and, as such, are subject to periodic changes as new information becomes available.

Product Revenue

Product revenue increased by $15,000, or approximately 9%, to $187,000 in the three months ended June 30, 2023 from $172,000 for the three months ended June 30, 2022.

Product revenue consisted of the sale of FreeHold Duo and Trio intracorporeal organ retractors and revenue is recognized when product is shipped to customers. The increase in product revenue was primarily due to a increase in the purchase volume of FreeHold Duo and Trio intracorporeal organ retractors. There were no changes to the per unit sale price in either period presented.

Cost of Product Revenue

Cost of product revenue decreased by $6,000, or approximately 10%, to $54,000 in the three months ended June 30, 2023 from $60,000 for the three months ended June 30, 2022. The decrease was primarily due to decreased production costs of FreeHold Duo and Trio intracorporeal organ retractors.

Research and Development Expenses

The following table summarizes our research and development expenses for the three months ended June 30, 2023 and 2022 (in thousands):

	Three Months Ended June 30,	
	2023	2022
Personnel and consulting costs	3,868	2,030
Non-clinical development costs	3,871	2,517
Clinical development costs	760	482
Total research and development expenses	$ 8,499	$ 5,029

Research and development expenses increased by $3.5 million, or approximately 69%, to $8.5 million for the three months ended June 30, 2023, from $5.0 million for the three months ended June 30, 2022. This is primarily due to an increase in support of ongoing work to advance BackBeat CNT and Virtue SAB into planned pivotal studies during 2023 and included an increase in personnel related expenses of $1.4 million due to increased headcount and associated expenses, along with increased stock-based compensation of $399,000, an increase of $1.4 million in research and development program costs, supplies, and testing, and an increase of $278,000 in clinical development costs.

The total research and development expenses summarized above include $4.4 million for the three months ended June 30, 2023 and $3.8 million for the three months ended June 30, 2022 related to the Terumo Agreement. The increase of $657,000 is due to increased expense activity related to the Terumo Agreement during the 2023 period.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $2.4 million, or approximately 81%, to $5.3 million for the three months ended June 30, 2023, from $2.9 million of expense for the three months ended June 30, 2022. The increase was primarily due to an increase in stock-based compensation of $1.1 million, and an increase of $691,000 of accounting, finance, legal expenses, investor relations and public relations expenses incurred in connection with the overall growth of the business and in preparation for becoming and being a public company.

Interest Income (Expense), Net

Interest income (expense), net, increased by $1.2 million, or approximately 483%, to $941,000 of income for the three months ended June 30, 2023, from $246,000 of expense for the three months ended June 30, 2022. The net interest income in the 2023 period

consisted primarily of interest earned from marketable securities offset by monthly interest expense incurred resulting from the 2022 Loan and Security Agreement. The net interest expense in the 2022 period consisted primarily of interest expense incurred resulting from the December 31, 2020 drawdown of the $10.0 million tranche from the 2019 Loan and Security Agreement.

Loss on Fair Value Adjustment of Warrant Liability

The loss on fair value adjustment of warrant liability was a loss of $1.0 million for the three months ended June 30, 2022. There were no additional charges for the adjustment of fair value for warrant liability in the three months ended June 30, 2023 as it had been settled in the first quarter with the close of the Business Combination.

Loss on Debt Extinguishment

The loss on debt extinguishment was $682,000 for the three months ended June 30, 2022. The loss was due to recognition of unamortized debt discount as well as early termination payments related to the early termination and repayment of the existing 2019 Loan and Security Agreement in June 2022.

(Loss) Gain on Fair Value of Strategic Investments

The loss in fair value of strategic investments was $31,000 for the three months ended June 30, 2023, as compared to a gain of $1.7 million for the three months ended June 30, 2022. The amounts recognized for the three months ended June 30, 2023 related to the change in fair value in our common stock holdings of Motus GI. The amount recognized for the three months ended June 30, 2022, relates to a gain on our strategic investment in Vivasure of $1.9 million, partially offset by the change in fair value in our common stock holdings of Motus GI. The gain on our strategic investment in Vivasure was attributable to an observable price change for an identical investment due to a new third-party investment. Therefore, the investment was measured at fair value and a gain was recognized.

Comparison of the Years Ended December 31, 2022 and 2021

The following table presents Legacy Orchestra’s statements of operations for the years ended December 31, 2022 and 2021, and the dollar and percentage change between the two years (in thousands):

	Year Ended December 31,			
	2022	2021	Change $	Change %
Revenue:				
Partnership revenue	$ 2,862	$ (1,475)	$ 4,337	294%
Product revenue	671	693	(22)	(3)%
Total revenue	3,533	(782)	4,315	552%
Expenses:				
Cost of product revenue	211	199	12	6%
Research and development	21,945	12,890	9,055	70%
Selling, general and administrative	14,034	7,928	6,106	77%
Total expenses	36,190	21,017	15,173	72%
Loss from operations	(32,657)	(21,799)	(10,858)	(50)%
Other income (expense):				
Interest (expense) income, net	50	(927)	977	105%
Gain (loss) on fair value adjustment of warrant liability	(1,350)	699	(2,049)	(293)%
Loss on debt extinguishment	(682)	—	(682)	NM[1]
(Loss) gain on fair value of strategic investments	1,031	(987)	2,018	204%
Total other expense	(951)	(1,215)	264	22%
Net loss	$ (33,608)	$ (23,014)	$ (10,594)	(46)%

(1) Amount is not meaningful

Partnership Revenue

Partnership revenue increased by $4.3 million, or 294%, from ($1.5) million in 2021 to $2.9 million in 2022. Partnership revenue relates to the recognition of the combined performance obligation for the license granted to Terumo and the ongoing research and development services over the estimated performance period for the Virtue SAB coronary ISR indication, using a proportional performance model, based on the costs incurred relative to the total estimated costs of the research and development services. As of each quarterly reporting date, Orchestra evaluates its estimates of the total costs expected to be incurred through the completion of the combined performance obligation and updates its estimates as necessary.

For the years ended December 31, 2021 and 2022, the expenses incurred related to the Terumo Agreement were approximately $9.9 million and $14.3 million, respectively. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 85% as of December 31, 2021 as compared to the estimates as of December 31, 2020, and increased by approximately 10% as of December 31, 2022, as compared to the estimates as of December 31, 2021. The increase in the estimated costs relates to an extension of the estimated performance period by twelve months, due in part to delays resulting from the COVID-19 pandemic, as well as supply chain issues and unexpected changes to regulatory requirements, including increased testing and other activities related to chemistry, manufacturing and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, that caused the Company to amend its original project plan. While Orchestra believes it has estimated total costs associated with the Terumo Agreement through completion, these estimates encompass a broad range of expenses over a multi-year period and, as such, are subject to periodic changes as new information becomes available.

Product Revenue

Product revenue decreased by $22,000, or 3%, from $693,000 in 2021 to $671,000 in 2022. The decrease was primarily due to a decrease in the purchase volume of FreeHold Duo and Trio intracorporeal organ retractors. There have been no changes to the per unit sale price in either period presented. Product revenue consisted of the sale of FreeHold Duo and Trio intracorporeal organ retractors and revenue is recognized when product is shipped to customers.

Cost of Product Revenue

Cost of product revenue increased by $12,000, or 6%, from $199,000 in 2021 to $211,000 in 2022. The increase was primarily due to increased production costs of FreeHold Duo and Trio intracorporeal organ retractors.

Research and Development Expenses

The following table summarizes Orchestra’s research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

	Years Ended December 31,	
	2022	2021
Personnel and consulting costs	$ 9,442	$ 6,539
Research and development program costs, supplies and testing	9,175	4,139
Clinical development costs	1,932	742
Other research and development costs	1,396	1,470
Total research and development expenses	$ 21,945	$ 12,890

Research and development expenses increased by $9.1 million, or 70%, from $12.9 million in 2021 to $21.9 million in 2022. This was primarily due to an increase of $5.0 million in animal study and drug formulation development costs. There was also an increase in personnel related expenses of $2.9 million due to increased headcount and associated expenses.

The total research and development expenses summarized above include $9.1 million in 2021 and $13.9 million in 2022 related to the Terumo Agreement. The increase of $4.8 million is due to increased expense activity related to the Terumo Agreement during the 2022 period.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $6.1 million, or 77%, from $7.9 million in 2021 to $14.0 million in 2022. The increase was primarily due to an increase in headcount which resulted in a $2.1 million increase in salary and medical benefit costs, along with increased stock-based compensation of $2.7 million, increased outside consultant expenses of $499,000 and $464,000 of accounting, finance and legal expenses incurred in connection with the overall growth of the business and in preparation for becoming a public company.

Interest (Expense) Income, Net

Interest (expense) income, net, increased by $977,000, or 105%, from $927,000 of expense in 2021 to $50,000 of income in 2022. The net interest expense in 2021 consisted primarily of interest expense incurred resulting from the December 31, 2020 drawdown of the $10.0 million tranche from the termination of the 2019 Loan and Security Agreement. The net interest income in 2022 consisted primarily of monthly interest incurred resulting from the 2019 Loan and Security Agreement and interest expense incurred resulting from the 2022 Loan and Security Agreement through September 2022 offset by interest earned from marketable securities.

Gain (Loss) on Fair Value Adjustment of Warrant Liability

The gain on fair value adjustment of warrant liability was $699,000 in 2021 as compared to a loss of $1.4 million in 2022. The change year over year is primarily a result of an amendment to the terms of certain existing warrant agreements, which included modifying the underlying shares of the warrants from preferred warrants to common warrants and reducing the strike prices. Such amendments resulted in $810,000 of additional expense for the year ended December 31, 2022. Further, the change in the fair value of our outstanding warrants due to an increase in the fair value of the underlying common and preferred stock resulted in $578,000 of additional expense for year ended December 31, 2022.

Loss on Debt Extinguishment

The loss on debt extinguishment was $682,000 for 2022. The loss was due to recognition of unamortized debt discount as well as the early termination payment related to the early termination and repayment of the 2019 Loan and Security Agreement in June 2022.

(Loss) Gain on Fair Value of Strategic Investments

The loss on fair value of strategic investments was $1.0 million in 2021, as compared to a gain of $1.0 million for 2022. The amount recognized in 2021 related to the change in fair value in our common stock holdings of Motus GI. The amount recognized in 2022 relates to a gain on our strategic investment in Vivasure of $1.9 million, partially offset by the change in fair value in our common stock holdings of Motus GI. The gain on our strategic investment in Vivasure is attributable to an observable price change for an identical investment due to a new third-party investment. Therefore, the investment is measured at fair value and a gain was recognized.

Liquidity and Capital Resources

From inception through June 30, 2023, we have incurred significant operating losses and negative cash flows from our operations. Legacy Orchestra’s net losses were $23.0 million and $33.6 million for the years ended December 31, 2021 and 2022, respectively. Our net losses were $23.0 million and $13.6 million for the six months ended June 30, 2023 and June 30, 2022, respectively. As of June 30, 2023, we had an accumulated deficit of $222.7 million. We have funded our operations primarily through the issuance of convertible preferred stock and proceeds from the Business Combination, as well as through proceeds from the Terumo Agreement, borrowings under debt arrangements and, to a lesser extent, from FreeHold product revenue. We have raised a cumulative approximately $166.8 million in gross proceeds through the issuance of convertible preferred stock, approximately $70.0 million in gross proceeds from the Business Combination, and have received $30.0 million under the Terumo Agreement through June 30, 2023. We had $16.4 million in cash and cash equivalents at June 30, 2023, which consisted primarily of bank deposits and money market funds. We also had $101.3 million of short-term marketable securities at June 30, 2023, which consisted primarily of our investments in corporate and government debt securities.

Funding Requirements

We expect our operating expenses to increase significantly as we continue to develop and seek regulatory approvals and along with our partners, prepare for potential commercialization of our product candidates. Our research and development spending is expected to increase from historical levels during 2023 as we perform enabling work in preparation for the BackBeat CNT and Virtue SAB pivotal studies, commence enrollment of both planned studies and execute additional planned research and development activities. In addition, we expect our selling, general and administrative expenses to increase due to increases in headcount along with expenses associated with being a public company.

Based on current clinical development and other research and development plans and budget estimates, we anticipate that our cash and cash equivalents and marketable securities are sufficient to fund our operations into 2026. The amount and timing of our future funding requirements may change from current estimates and will depend on many factors, including the cost and pace of execution of clinical studies and research and development activities, the strength of results from clinical studies for our flagship product candidates and other research, development, manufacturing and commercial activities as well as the potential receipt of revenues under the Terumo Agreement, the Medtronic Agreement and/or future collaborations. We may seek additional funding through the issuance of new equity, may make drawdowns on our existing or new loan facilities, may receive milestone payments from the Terumo Agreement or through payments from collaborations or partnerships with other companies, and/or may realize cash from the sale of some or all of our strategic holdings, although there are no assurances in this regard.

Cash Flows

The following table summarizes Orchestra’s cash flow data for the periods indicated (in thousands):

	Six Months Ended June 30,	
	2023	2022
Net cash used in operating activities	$ (24,871)	$ (13,289)
Net cash used in investing activities	(35,411)	(521)
Net cash provided by financing activities	56,907	110,845
Net (decrease) increase in cash and cash equivalents	$ (3,375)	$ 97,035

Comparison of the Six Months Ended June 30, 2023 and 2022

Net Cash Flows from Operating Activities

Net cash used in operating activities for the six months ended June 30, 2023 was $24.9 million and primarily consisted of our net loss of $23.0 million and changes in net operating assets and liabilities of $3.8 million, which was offset by non-cash charges of $1.9 million. Our non-cash charges primarily consisted of a loss on fair value adjustment of warrant liability of $294,000 and stock-based compensation of $3.2 million, offset by $2.1 million related to accretion and interest of marketable securities. The net change in operating assets and liabilities were primarily due to a decrease in accounts payable and accrued expenses of $1.0 million, an increase in prepaid expenses and other assets of $723,000, and a decrease in deferred revenue of $1.7 million and various other immaterial changes.

Net cash used in operating activities for the six months ended June 30, 2022, was $13.3 million and primarily consisted of our net loss of $13.6 million, and changes in net operating assets and liabilities of $830,000, which was offset by non-cash charges of $1.1 million. Our non-cash charges primarily consisted of a loss on fair value adjustment of warrant liability of $1.2 million, loss on debt extinguishment of $682,000, stock-based compensation of $289,000, amortization of deferred financing costs of $91,000 and non-cash lease expense of $269,000, offset by a $1.5 million gain on the fair value of strategic investments. The net change in operating assets and liabilities were primarily due to a decrease in deferred revenue of $945,000 and an increase in prepaid expenses and other assets of $485,000, offset by an increase in accounts payable, accrued expenses and other liabilities of $672,000 and various other immaterial changes.

Net Cash Flows from Investing Activities

Net cash used in investing activities for the six months ended June 30, 2023 was $35.4 million, which primarily consisted of the purchase of $99.5 million of marketable securities offset by the sale of $64.2 million of marketable securities.

Net cash used in investing activities for the six months ended June 30, 2022, was $521,000, which consisted of the purchase of $313,000 of property and equipment and the purchase of $208,000 of strategic investments.

Net Cash Flows from Financing Activities

Net cash provided by financing activities of $56.9 million for the six months ended June 30, 2023 was primarily attributable to net proceeds from the Business Combination.

Net cash provided by financing activities of $110.8 million for the six months ended June 30, 2022, was attributable to gross proceeds from the Series D-1 private equity financing, and the Series D-2 private equity financing totaling $110 million, and proceeds from the 2022 Loan and Security Agreement with Avenue of $10 million. These proceeds were offset by $2.7 million of deferred financing costs and principal repayment of $6.4 million, inclusive of debt extinguishment costs, from the termination of the 2019 Loan and Security Agreement with Silicon Valley Bank.

Comparison of the Years Ended December 31, 2022 and 2021

Net Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $29.3 million and primarily consisted of our net loss of $33.6 million, and changes in net operating assets and liabilities of $450,000, which was offset by non-cash charges of $4.7 million. Our non-cash charges primarily consisted of a loss on fair value adjustment of warrant liability of $1.4 million, loss on debt extinguishment of $682,000, stock-based compensation of $3.4 million, amortization of deferred financing costs of $163,000 and non-cash lease expense of $571,000, offset by a $1.0 million gain on the fair value of investments and $600,000 related to accretion and interest of marketable securities. The net change in operating assets and liabilities were primarily due to a decrease in deferred revenue of $2.9 million, an increase in prepaid expenses and other assets of $439,000, and an increase in inventory of $208,000, offset by an increase in accounts payable, accrued expenses and other liabilities of $3.4 million and various other immaterial changes.

Net cash used in operating activities for the year ended December 31, 2021 was $19.4 million and primarily consisted of our net loss of $23.0 million, which was offset by non-cash charges of $1.0 million and changes in net operating assets and liabilities of $2.6 million. Legacy Orchestra’s non-cash charges primarily consisted of a $1.0 million adjustment in fair value of strategic investments, stock-based compensation of $302,000, and amortization of deferred financing fees of $217,000, partially offset by a gain on fair value adjustment of warrant liability of $699,000. The net change in operating assets and liabilities were primarily due to an increase in deferred revenue of $1.5 million related to the extension of the expected timeline and increasing budgeted costs of the performance obligation from the Terumo Agreement during the year and an increase of $1.1 million in accounts payable and accrued expenses due to timing of vendor payments.

Net Cash Flows from Investing Activities

Net cash used in investing activities for the year ended December 31, 2022, was $64.1 million, which consisted of the purchase of $63.3 million of marketable securities, $591,000 of property and equipment and $208,000 of strategic investments.

Net cash provided by investing activities for the year ended December 31, 2021 was $13.0 million, which primarily consisted of the sale of $13.5 million of marketable securities, partially offset by the purchase of property and equipment for $274,000 and the purchase of unsecured convertible redeemable loan notes and accumulated interest from Vivasure for $213,000.

Net Cash Flows from Financing Activities

Net cash provided by financing activities of $103.3 million for the year ended December 31, 2022 was attributable to gross proceeds from Legacy Orchestra’s Series D-1 private equity financing (the “Series D-1 Financing”), and the Series D-2 Financing

totaling $110 million, and proceeds from the 2022 Loan and Security Agreement of $10 million. These proceeds were offset by $10.3 million of deferred financing and offer costs and principal repayment of $6.4 million, inclusive of debt extinguishment costs, from the termination of the 2019 Loan and Security Agreement to Silicon Valley Bank.

Net cash used in financing activities of $4.0 million for the year ended December 31, 2021 was primarily related to the principal repayment of $4.0 million from the 2019 Loan and Security Agreement to Silicon Valley Bank.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments as of June 30, 2023 (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating lease obligations	$ 2,284	$ 833	$ 835	$ 616	$ —
Debt, principal and interest[(1)]	13,776	1,495	12,281	—	—
Total	$ 16,060	$ 2,328	$ 13,116	$ 616	$ —

(1) In June 2022, Legacy Orchestra entered into the 2022 Loan and Security Agreement with Avenue. As part of the 2022 Loan and Security Agreement, Legacy Orchestra paid off the balance of the 2019 Loan and Security Agreement with Silicon Valley Bank. On October 6, 2023, the 2022 Loan and Security Agreement was repaid in full and terminated. Refer to Note 14, Debt Financing, to our Condensed Consolidated Financial Statements.

The following table summarizes Legacy Orchestra's contractual obligations and commitments as of December 31, 2022 (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating lease obligations	$ 2,694	$ 823	$ 1,079	$ 704	$ 88
Debt, principal and interest[(1)]	14,328	1,414	9,491	3,423	—
Total	$ 17,022	$ 2,237	$ 10,570	$ 4,127	$ 88

(1) In June 2022, Legacy Orchestra entered into the 2022 Loan and Security Agreement with Avenue. As part of the 2022 Loan and Security Agreement, Legacy Orchestra paid off the balance of the 2019 Loan and Security Agreement with Silicon Valley Bank. On October 6, 2023, the 2022 Loan and Security Agreement was repaid in full and terminated. Refer to Note 14, Debt Financing, to our Condensed Consolidated Financial Statements.

In addition, we enter into agreements in the normal course of business with clinical research organizations for work related to clinical trials and with vendors for preclinical studies and other services and products for operating purposes, which are cancelable at any time by us, generally upon 30 days prior written notice. These payments are not included in the above table of contractual obligations and commitments.

Critical Accounting Policies and Estimates

Our financial statements are prepared in accordance with U.S. GAAP. The preparation of the financial statements in conformity with U.S. GAAP requires our management to make a number of estimates and assumptions relating to the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the period. We evaluate our significant estimates on an ongoing basis, including estimates related to the total costs expected to be incurred though the completion of the combined performance obligation of the Terumo Agreement, research and development prepayments, accruals and related expenses and stock-based compensation. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

We believe that the accounting policies described below involve a significant degree of judgment and complexity. Accordingly, we believe these are the most critical to aid in fully understanding and evaluating our financial condition and results of operations. For further information, see Note 2 to our Condensed Consolidated Financial Statements.

Revenue Recognition

We recognize revenue under the core principle according to ASC 606 to depict the transfer of control to our customers in an amount reflecting the consideration we expect to be entitled to. In order to achieve that core principle, we apply the following five step approach: (1) identify the contract with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when a performance obligation is satisfied.

Our revenues are currently comprised of product revenue from the sale of FreeHold's intracorporeal organ retractors and partnership revenues under the Terumo Agreement related to the development and commercialization of Virtue SAB.

Product Revenues

Product revenues related to sales of FreeHold's intracorporeal organ retractors are recognized at a point-in-time upon the shipment of the product to the customer, and there are no significant estimates or judgments related to estimating the transaction price. The product revenues consist of a single performance obligation, and the payment terms are typically 30 days. Product revenues are recognized solely in the United States.

Partnership Revenues

To date, our partnership revenues have related to the Terumo Agreement described below. In future periods, partnership revenues may also include revenues related to the Medtronic Agreement.

Legacy Orchestra entered into the Terumo Agreement as further described in Note 4 to our Condensed Consolidated Financial Statements. We assessed whether the Terumo Agreement fell within the scope of ASC 808 based on whether the arrangement involved joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. We determined that the Terumo Agreement did not fall within the scope of ASC 808. We then analyzed the arrangement pursuant to the provisions of ASC 606 and determined that the arrangement represents a contract with a customer and is therefore within the scope of ASC 606.

The promised goods or services in the Terumo Agreement include (i) license rights to our intellectual property and (ii) research and development services. We also have optional additional items in the Terumo Agreement, which are considered marketing offers and are accounted for as separate contracts with the customer if such option is elected by the customer, unless the option provides a material right which would not be provided without entering into the contract. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources or (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct in the Terumo Agreement, we considered factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

We estimate the transaction price for the Terumo Agreement performance obligations based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration includes both fixed consideration and variable consideration. At the inception of the Terumo Agreement, as well as at each reporting period, we evaluate the amount of potential payment and the likelihood that the payments will be received. We utilize either the most likely amount method or expected amount method to estimate the amount expected to be received based on which method better predicts the amount expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

The Terumo Agreement contains development and regulatory milestone payments. At contract inception and at each reporting period, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the

transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect partnership revenues and earnings in the period of adjustment.

The Terumo Agreement also includes sales-based royalties and the license is deemed to be the predominant item to which the royalties relate. Accordingly, we will recognize royalty revenue when the related sales occur. To date, we have not recognized any royalty revenue under the arrangement.

We have determined that intellectual property licensed to Terumo and the research and development services to be provided through the premarket approval by the FDA for the ISR indication represent a combined performance obligation that is satisfied over time, and that the appropriate method of measuring progress for purposes of recognizing revenues relates to a proportional performance model that measures the proportional performance based on the costs incurred to date relative to the total costs expected to be incurred through the completion of the performance obligation. We evaluate the measure of progress at each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

In the six months ended June 30, 2023, we updated our estimates of the total costs expected to be incurred through the completion of the combined performance obligation. The impact of the changes in estimates resulted in a reduction in partnership revenues of $303,000, which resulted in a $0.01 effect on net loss per share, basic and diluted. In the six months ended June 30, 2022, the impact of the changes in estimates resulted in a reduction in partnership revenues of $847,000, which resulted in a $0.05 effect on net loss per share, basic and diluted.

In 2021, we updated our estimates of the total costs expected to be incurred through the completion of the combined performance obligation. The impact of the changes in estimates resulted in a reduction of partnership revenues of $6.5 million, or a net loss per share, basic and diluted, of $0.73. In 2022, the impact of the changes in estimates resulted in a reduction of partnership revenues of $1.0 million, or a net loss per share, basic and diluted, of $0.07.

We receive payments from Terumo based on billing schedules established in the contract. Such billings for milestone related events have 10-day terms from the date the milestone is achieved, royalty payments are 20-day terms after the close of each quarter, any optional services are 20 days after receipt of an invoice and sales of the SirolimusEFR are within 30 days after receipt of the shipping invoices. Upfront payments are recorded as deferred revenue upon receipt or when due until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when the right to consideration is unconditional.

In June 2022, Legacy Orchestra, BackBeat Medical, LLC and Medtronic entered into the Medtronic Agreement for the development and commercialization of BackBeat CNT for the treatment of HTN in patients indicated for a cardiac pacemaker. We determined that the arrangement is a collaboration within the scope of ASC 808. In addition, we concluded Medtronic is a customer for a good or service that is a distinct unit of account, and therefore the transactions in the Medtronic Agreement should be accounted for under ASC 606. Through June 30, 2023, there have been no amounts recognized as revenue under the Medtronic Agreement.

Research and Development Prepayments, Accruals and Related Expenses

We incur costs of research and development activities conducted by our third-party service providers, which include the conduct of preclinical and clinical studies. We are required to estimate our prepaid and accrued research and development costs at each reporting date. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with our service providers. We determine the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers, as to the progress or stage of completion of trials or services, as of the end of the reporting period, pursuant to contracts with the third parties and the agreed upon fee to be paid for such services. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are accepted by us or the services are performed. Accruals are recorded for the amounts of services provided that have not yet been invoiced.

Warrants

We evaluate our warrants to determine if the contracts qualify as liabilities in accordance with ASC 480-10, *Distinguishing Liabilities from Equity*, and ASC 815, *Derivatives and Hedging*. If the warrant is determined to meet the criteria to be liability classified, the warrant liability is marked-to-market each balance sheet date and recorded as a liability, with the change in fair value recorded in our condensed consolidated statements of operations and comprehensive loss as gain (loss) on fair value adjustment of warrant liability within other income or expense.

In bundled transactions, the proceeds received from any debt instruments and liability classified warrants are allocated to the warrant at fair value first, and the residual value is then allocated to the debt instrument. Upon conversion or exercise of a warrant that is subject to liability treatment, the instrument is marked to fair value at the conversion or exercise date and the fair value is reclassified to equity. Equity classified warrants are recorded within additional paid-in capital at the time of issuance at fair value as of the issuance date and are not subject to subsequent remeasurement.

Stock-Based Compensation

We account for share-based payments at fair value. The fair value of stock options is measured using the Black-Scholes option-pricing model and the fair value of restricted stock is measured based on the fair value of the Common Stock underlying the award as of the grant date, described further below. For share-based awards that vest subject to the satisfaction of a service requirement, the fair value measurement date for stock-based compensation awards is the date of grant and the expense is recognized on a straight-line basis, over the vesting period. We account for forfeitures as they occur.

Prior to the Business Combination, due to the absence of an active market for Legacy Orchestra’s common stock, Legacy Orchestra utilized methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants’ Audit and Accounting Practice Guide: Valuation of Privately-Held Company Equity Securities Issued as Compensation to estimate the fair value of its common stock. The fair value of Legacy Orchestra’s common stock was determined based upon a variety of factors, including valuations of Legacy Orchestra’s common stock performed with the assistance of independent third-party valuation specialists; Legacy Orchestra’s stage of development and business strategy, including the status of research and development efforts of its product candidates, and the material risks related to its business and industry; Legacy Orchestra’s business conditions and projections; Legacy Orchestra’s results of operations and financial position, including its levels of available capital resources; the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies; the lack of marketability of Legacy Orchestra’s common stock as a private company; the prices of Legacy Orchestra’s convertible preferred stock sold to investors in arm’s length transactions and the rights, preferences and privileges of its convertible preferred stock relative to those of its common stock; the likelihood of achieving a liquidity event for the holders of Legacy Orchestra’s common stock, such as an initial public offering or a sale of Legacy Orchestra given prevailing market conditions; trends and developments in its industry; the hiring of key personnel and the experience of management; and external market conditions affecting the life sciences and biotechnology industry sectors. Significant changes to the key assumptions underlying the factors used could result in different fair values of Legacy Orchestra’s common stock at each valuation date. In determining the exercise prices for options granted and fair value of restricted stock, we have considered the fair value of the common stock as of the grant date.

Prior to the Business Combination, valuation analyses were conducted utilizing a probability weighted expected return method, in which the probability of a public company scenario was considered via either an initial public offering or special purpose acquisition company transaction. Subsequent to the Business Combination, fair value was determined by market prices of the Common Stock of the Company.

We classify stock-based compensation expense in our condensed consolidated statements of operations and comprehensive loss in the same manner in which the award recipients’ payroll costs are classified or in which the award recipients’ service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option pricing model, which is based on the assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

- *Expected Term* — The expected term represents the period that stock-based awards are expected to be outstanding. Our historical share option exercise information is limited due to a lack of sufficient data points and does not provide a reasonable basis upon which to estimate an expected term. The expected term for option grants is therefore determined using the "simplified" method, as prescribed in the SEC's Staff Accounting Bulletin No. 107. The simplified method deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards.

- *Expected Volatility* — The expected volatility was derived from the historical stock volatilities of comparable *peer* public companies within our industry that are considered to be comparable to our business over a period equivalent to the expected term of the stock-based awards, since there was no trading history of Legacy Orchestra's common stock and limited trading history of the Company.

- *Risk-Free Interest Rate* — The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the stock-based awards' expected term.

- *Expected Dividend Yield* — The expected dividend yield is zero as neither the Company nor Legacy Orchestra has paid, *and* we do not anticipate paying, any dividends on the Common Stock of the Company in the foreseeable future.

- *Common Stock Valuation* — Prior to the Business Combination, given the absence of a public trading market for Legacy Orchestra's common stock, Legacy Orchestra's board of directors considered numerous subjective and objective *factors* to determine the best estimate of fair value of Legacy Orchestra's common stock underlying the stock options granted to its employees and non-employees. In determining the grant date fair value of Legacy Orchestra's common stock, Legacy Orchestra's board considered, among other things, contemporaneous valuations of its common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Following the Business Combination, our Board determines the fair value of the Common Stock of the Company based on the closing price of the Common Stock of the Company on or around the date of grant.

During the years ended December 31, 2022 and 2021, stock-based compensation was $3.4 million and $302,000, respectively. During the six months ended June 30, 2023 and 2022, stock-based compensation was $3.2 million and $289,000, respectively. As of June 30, 2023, we had approximately $6.6 million of total unrecognized stock-based compensation, which we expect to recognize over a weighted-average period of approximately 3 years.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our Condensed Consolidated Financial Statements.

Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents and marketable securities as of December 31, 2022 and June 30, 2023 consisted of $83.7 million and $117.7 million, respectively, in bank deposits, money market funds and corporate and government debt instruments. Such interest-earning instruments carry a degree of interest rate risk. The goals of our investment policy are liquidity and capital preservation; we do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate exposure. We believe that we do not have any material exposure to changes in the fair value of these assets as a result of changes in interest rates due to the short-term nature of our cash and cash equivalents and marketable securities.

Inflation Risk

Inflation could affect us by increasing its cost of labor and clinical study costs. Orchestra does not believe that inflation has had a material effect on its business, financial condition, or results of operations during the periods presented.

Emerging Growth Company and Smaller Reporting Company Status

We are an "emerging growth company," as defined in Section 2(a) of the Securities Act, as modified by the JOBS Act. As such, we are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in its periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Further, Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a Securities Act registration statement declared effective or do not have a class of securities registered under the Exchange Act) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that an emerging growth company can elect to opt out of the extended transition period and comply with the requirements that apply to non-emerging growth companies but any such election to opt out is irrevocable. We have elected not to opt out of such extended transition period which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of our financial statements with another public company which is neither an emerging growth company nor an emerging growth company which has opted out of using the extended transition period difficult or impossible because of the potential differences in accounting standards used.

We will remain an emerging growth company until the earliest of (1) the last day of the fiscal year following the fifth anniversary of the closing of the initial public offering of HSAC2, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of the Common Stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year, or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) the market value of our voting and non-voting Common Stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or (ii)(a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting Common Stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

BUSINESS

Our Vision

Our vision is to accelerate medical innovation to patients through risk-reward-sharing partnerships with leading medical device companies.

Our Company

We are a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. Our partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products it develops. We are led by a highly accomplished, multidisciplinary management team and a board of directors with extensive experience in all phases of therapeutic device development. Our business was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by its founding team. Our flagship product candidates are BackBeat CNT for the treatment of hypertension, the leading risk factor for death worldwide, and Virtue SAB for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide.

BackBeat CNT, also known as Atrioventricular Interval Modulation ("AVIM") therapy, is a bioelectronic therapy candidate designed to substantially and persistently lower blood pressure that can be fully integrated as a firmware upgrade to standard cardiac pacemakers, although there is no guarantee BackBeat CNT will be safe and effective. BackBeat CNT showed encouraging results in MODERATO II, a prospective, multi-center, randomized, double-blind pilot study of pacemaker patients with persistent HTN. HTN is the most common comorbidity in this population, affecting over 70% of the pacemaker-indicated patients. We estimate that the addressable annual market for pacemaker-indicated patients with HTN will comprise more than 750,000 patients worldwide by 2025 and represents a potential annual revenue opportunity of over $2 billion. We also believe BackBeat CNT may offer therapeutic benefit to select high-risk HTN patients not indicated for a pacemaker. We estimate that this additional addressable annual market for high-risk HTN patients will comprise more than 2.4 million patients worldwide by 2025 and represents a potential annual revenue opportunity of more than $8 billion.

On September 19, 2023, we announced that the FDA granted us IDE approval to initiate our planned BACKBEAT pivotal study of BackBeat CNT (AVIM therapy) to treat hypertension in patients indicated for a pacemaker. We currently expect to initiate enrollment of the BACKBEAT pivotal study before the end of 2023 following completion of clinical trial initiation activities including clinical center Institutional Review Board approvals.

On June 30, 2022, we entered into an exclusive license and collaboration agreement with Medtronic, one of the largest medical device companies in the world, for the development of BackBeat CNT for the treatment of HTN in pacemaker-indicated patients (the "Medtronic Collaboration"). The Medtronic Collaboration provides us with development, clinical and regulatory support for the BACKBEAT pivotal study. Upon regulatory approval, if received, Medtronic will have the exclusive global rights to commercialize BackBeat CNT (AVIM therapy) for this target population. If BackBeat CNT is approved and successfully commercialized, we will share meaningfully in the revenues generated from Medtronic's sale of BackBeat CNT-enabled pacing systems. Medtronic has a right of first negotiation with respect to BackBeat CNT for the treatment of HTN in non-pacemaker patients.

Virtue SAB is a proprietary drug/device combination product candidate for the treatment of artery disease that is designed to deliver a proprietary, investigational, extended-release formulation of sirolimus ("SirolimusEFR"), to the vessel wall during balloon angioplasty without the need for balloon coating or a permanent implant, although there is no guarantee Virtue SAB will prove to be safe and effective. Virtue SAB demonstrated promising three-year clinical data in coronary ISR in the prospective, multi-center SABRE Study.

Virtue SAB was granted Breakthrough Device designation by the FDA, for specific indications relating to the treatment of coronary ISR, coronary small vessel disease and peripheral artery disease below-the-knee. We estimate that these indications will represent an annual global addressable market opportunity comprising approximately 3.2 million procedures and valued at approximately $3 billion, as discussed below under *"— FOCAL THERAPIES — Virtue SAB for Artery Disease and SirolimusEFR for Local Inflammation in Multiple Indications. —Targeted Unmet Needs and Market Opportunity for Virtue SAB."*

On August 8, 2023, we announced that the FDA granted us investigational device exemption approval with conditions to initiate our planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary ISR. The conditional approval permits us to initiate enrollment of the Virtue ISR-US pivotal study following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals. We are also required to submit additional information to the FDA.

We have a strategic partnership with Terumo, a global leader in medical technology, for the development and commercialization of Virtue SAB to treat CAD or PAD. Under the terms of our partnership, it is expected that Terumo will assume financial and execution responsibility for substantially all future clinical and regulatory development, with the exception of the Virtue ISR-US pivotal study, for which we are responsible. Terumo will also be responsible for device manufacturing, commercial sales, marketing and distribution for Virtue SAB for coronary and peripheral vascular indications globally. If Virtue SAB is successfully developed and approved, we will share meaningfully in future commercial revenues of Virtue SAB through double-digit royalties on net sales and per unit payments as the exclusive supplier of SirolimusEFR.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to the Terumo Agreement that could serve to restructure milestone payments as well as make other potential material modifications to the Terumo Agreement. Until we gain clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development, and commercialization plans for Virtue SAB may continue to be adversely impacted.

Both Medtronic and Terumo have made equity investments in us with long-term hold restrictions. Medtronic invested $40 million in Legacy Orchestra’s January 30, 2022 Series D preferred equity financing (the “Series D Financing”) and purchased $10 million of HSAC2’s ordinary shares in connection with the Business Combination. Terumo invested $2.5 million in the Legacy Orchestra Series B-1 preferred stock private placement and $2.5 million in the Series D Financing.

History of Caliber and BackBeat

We were incorporated in Delaware in January 2017 and were formed to acquire operating and other assets as well as to raise capital to support further development of acquired assets. We had limited activity in 2017. In May 2018, we concurrently completed a recapitalization and mergers with Caliber Therapeutics, Inc., a Delaware corporation that has, among other things, the rights to the Virtue SAB product candidate and BackBeat Medical, Inc., a Delaware corporation that has, among other things, the rights to the BackBeat CNT product candidate. Caliber Therapeutics, Inc. was incorporated in Delaware in October 2005 and began development of its lead product candidate, Virtue SAB, in 2008. BackBeat Medical, Inc. was incorporated in Delaware in January 2010 and began development of its lead product candidate, BackBeat CNT, that same year.

Conversion of Caliber and BackBeat Limited Liability Companies

On December 26, 2019, we completed the conversions of Caliber Therapeutics, Inc., a Delaware corporation, to Caliber Therapeutics, LLC, a Delaware limited liability company, and BackBeat Medical, Inc., a Delaware corporation, to BackBeat Medical, LLC, a Delaware limited liability company. References in this prospectus to “Caliber” refer to Caliber Therapeutics, Inc. prior to its conversion to a limited liability company and to Caliber Therapeutics, LLC after its conversion to a limited liability company, as applicable. References in this prospectus to “BackBeat” refer to BackBeat Medical, Inc. prior to its conversion to a limited liability company and to BackBeat Medical, LLC after its conversion to a limited liability company, as applicable.

Partnership-Enabled Business Model

Our business was formed specifically to pursue a partnership-enabled business model that seeks to apply the strategies typically used by the biopharmaceutical industry to the medical device market where product developers are currently challenged with the financial and execution burdens of also needing to commercialize the products they are developing.

Our goal is to accelerate and improve the likelihood of its product innovations reaching patients and providers worldwide by sharing the risks and rewards of developing and commercializing these product candidates with established multinational companies, such as Medtronic and Terumo. Using this approach, we believe we can pursue multiple potentially lucrative innovation opportunities by focusing its efforts and resources on advancing promising therapeutic solutions, such as Virtue SAB and BackBeat CNT, through

late-stage clinical research and regulatory approvals. Meanwhile, our partners secure substantial new prospective growth opportunities with the potential to reduce risk and expense while leveraging their existing infrastructure to bring our partnered product candidates to global markets quickly and efficiently if regulatory approval is obtained.

We believe our partnership-enabled business model can create value for its stakeholders and partners by:

- ***Optimizing development and commercialization*** of its product candidates by pairing its research and development strengths and capabilities with the established commercial infrastructure of our partners;

- ***Enhancing capital efficiencies*** by sharing costs and responsibilities with our partners; and

- ***Maximizing the potential of future profitability*** by seeking to create multiple long-term high-margin royalty and revenue sharing arrangements with our partners.

Our Product Pipeline

Our pipeline is comprised of innovative therapeutic product candidates that we believe have the potential for value creation using our partnership-enabled business model, led by our two flagship product candidates, BackBeat CNT and Virtue SAB. We believe our flagship product candidates have the potential to improve clinical outcomes and provide distinct commercial advantages within two of the largest and well-established global medical device markets: Virtue SAB in interventional devices to treat CAD and PAD, an overall global market that LSI & Fortune Business Insights, market research firms, valued at a $20.9 billion market worldwide in 2022; and BackBeat CNT in cardiac rhythm management implants, an overall global market that LSI & Grand View Research valued at a $18.0 billion market worldwide in 2022. Our pipeline also includes additional product candidates in development for other significant medical conditions that we believe are attractive candidates for value creation using its partnership-enabled business model.

Our flagship product candidates are based on platform technologies that each have late-stage lead clinical indications with attractive follow-on clinical indications that could add substantial future commercial potential. Moreover, our additional pipeline opportunities, such as Cardiac Neuromodulation Therapy (“CNT”) for heart failure, or potential treatment of clinical indications such as urology or osteoarthritis using SirolimusEFR, and the microporous AngioInfusion balloon technology used in the Virtue SAB leverage the same platform technologies and intellectual property already developed for its flagship product candidates. Generally, our product candidates target large, mature global markets in which there are several active multinational and regional corporations with established distribution capabilities in place. These product candidates are designed to potentially offer important clinical, health and economic benefits without changing established treatment paradigms such as physician techniques or patient referral and treatment patterns, providing a select strategic partner a potential means to differentiate their product portfolios from competitors, drive revenue growth and gain market share. Our strategic collaboration agreements with Medtronic for BackBeat CNT and Terumo for Virtue SAB demonstrate our ability to align with global market leaders for the long-term development and commercialization of our product candidates.

The following table summarizes our material pipeline programs organized by product platform, as well as target indications, development status, market opportunity, strategic partners/collaborators and next milestones.

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Advancing a High-Impact Pipeline

Product Platforms	Target Indications	Preclinical	Clinical Feasibility	Clinical Pivotal	Partner	Study Sponsor
BackBeat CNT™ (AVIM Therapy)	Hypertension (HTN) (pacing patients; HTN+P)	IDE Approved			Medtronic	Orchestra BioMed
	High-Risk HTN[2] (non-pacing patients)				Medtronic ROFN	
CNT - HF	Heart Failure					
Virtue® Sirolimus AngioInfusion™ Balloon (SAB)	Coronary In-Stent Restenosis (ISR)	IDE Approved & FDA Breakthrough[3]			TERUMO	Orchestra BioMed
	Coronary Small Vessel (SV)[1]	FDA Breakthrough[4]			TERUMO	TERUMO
	Below-the-Knee (BTK)[1]	FDA Breakthrough[5]			TERUMO	TERUMO
SirolimusEFR™ / Microporous Balloon	Urology, orthopedics, oncology & other					

(1) Plan to leverage existing coronary ISR data to support potential pivotal study, although there have only been limited discussions with the FDA or a comparable foreign regulator in this regard.

(2) Will seek to leverage data from the pilot and pivotal trials involving HTN in patients indicated for a cardiac pacemaker (the “HTN+P population” or the “Primary Field”) to support clinical and regulatory development for High-Risk HTN indication given that age and other demographic factors of the target population are expected to be similar, the type of hypertension treated will likely be isolated systolic hypertension which is predominant in the HTN+P population, and other co-morbidities are also expected to be common to both target populations. However, there have been no discussions with the FDA or a comparable foreign regulator in this regard.

(3) In August 2023, Orchestra announced that the FDA had granted it approval with conditions to initiate the planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary ISR. Virtue SAB has received Breakthrough Device Designation by the FDA for the balloon dilatation of the stenotic portion (up to 26 mm length) of a stented coronary artery (ISR) that is 2.25 to 4.0 mm in diameter, for the purpose of improving lumen diameter.

(4) Virtue SAB has received Breakthrough Device Designation by the FDA for the balloon dilatation of the de novo stenotic portion (up to 26mm in lesion length) of a native coronary artery of 2.0 mm to 2.5 mm in diameter (small coronary arteries), for the purpose of improving lumen diameter.

(5) Virtue SAB has received Breakthrough Device Designation by the FDA for the balloon dilatation of the stenotic portion (up to 18 mm length) of an infrapopliteal artery (P-3 segment or distal, below the knee, with reference vessel diameter (RVD) 2.25 - 4.0 mm), for the purpose of improving lumen diameter.

BIOELECTRONIC PRODUCT CANDIDATES — BackBeat CNT (AVIM Therapy) for Hypertension and CNT-HF for Heart Failure

We are developing bioelectronic therapies based on patented CNT technology. Our product candidates are designed to use standard active implantable cardiac rhythm management systems, such as pacemakers, with changes to firmware and software only. Our flagship product candidate of the Bioelectronic Therapies Group is BackBeat CNT, also known as AVIM therapy, a patented, potential bioelectronics treatment for HTN, a significant risk factor for death worldwide. We have an exclusive strategic collaboration with Medtronic for the development and commercialization of BackBeat CNT for the treatment of hypertension in patients indicated for a cardiac pacemaker.

We are also pursuing CNT-HF, a bioelectronic product candidate that aims to reduce chronic sympathetic nervous system activity in heart failure (“HF”) for which there is an estimated global patient population of 64 million people according to the AME Medical Journal.

BackBeat Cardiac Neuromodulation Therapy (CNT) Product Candidate

In the discussion below and elsewhere in this prospectus, we reference p-values, which are statistical calculations that relate to the probability that the observed difference between groups happened by chance, with a p-value of less than 0.05 (i.e., less than 5% probability that the observed difference happened by chance) generally considered as the threshold to indicate statistical significance in clinical trials.

BackBeat CNT is now also known as Atrioventricular Interval Modulation or "AVIM" therapy. As such, the terms "BackBeat CNT" and "AVIM therapy" are used interchangeably below. With respect to the strategic collaboration agreement with Medtronic described below and the preclinical and clinical results also described below, the therapy is typically referred to as BackBeat CNT as this was term generally used to describe the therapy for such agreement or prior development activities. With respect to the BACKBEAT pivotal study we plan to initiate in the near future, the therapy is referred to as AVIM therapy.

BackBeat CNT is a bioelectronic product candidate for HTN that is designed to substantially reduce blood pressure. BackBeat CNT is delivered through programmed cardiac pacing algorithms and is designed to leverage standard rhythm management device procedures (dual-chamber pacemaker), utilizing the same implant procedure and lead positions while still enabling standard rhythm management (pacing) functions. While BackBeat CNT is designed to achieve certain results as described above, there is no guarantee that BackBeat CNT will prove to be safe and effective.

Clinical studies performed to date have been conducted using our proprietary Moderato system, a pacemaker system, incorporating BackBeat CNT. Clinical results from two European clinical studies, the MODERATO I single-arm clinical study and the MODERATO II double-blind, randomized, controlled pilot study, demonstrated a significant and clinically meaningful reduction in systolic blood pressure in hypertensive patients also indicated for a pacemaker. In particular, the MODERATO II study met its primary efficacy endpoint, as patients randomized to BackBeat CNT showed a statistically significant 11.1 mmHg ($p<0.01$) reduction in mean 24-hour ambulatory systolic blood pressure ("aSBP") at six months follow-up from activation, resulting in a statistically significant difference of 8.1 mmHg ($p=0.01$) of aSBP compared to control patients who were managed only with antihypertensive medications. The study also met its primary safety endpoint with no clinically meaningful differences in rate of MACE between the two groups at six months follow-up. Further details on the results of the BackBeat CNT clinical studies performed to date are provided below.

Strategic Collaboration Agreement with Medtronic

In June 2022, we and Medtronic entered into the Medtronic Agreement for the development and commercialization of BackBeat CNT for the treatment of HTN in patients indicated for a cardiac pacemaker (the "HTN+P population" or the "Primary Field"). Under the terms of the Medtronic Agreement, we are the sponsor for the BACKBEAT pivotal study to support regulatory approval in the United States, EU, Japan and other potential territories of AVIM therapy in the Primary Field and we are financially responsible for development, clinical and regulatory costs associated with this pivotal study.

Medtronic has completed integration and associated validation and verification testing of AVIM therapy algorithms as a field downloadable addition to its premium, commercially available dual-chamber pacemaker systems for use in the pivotal study. Medtronic is also providing clinical and regulatory resources in support of the pivotal study. We are reimbursing Medtronic at cost for these development, clinical and regulatory resources. Medtronic will integrate AVIM therapy, at our cost, as a firmware component of a premium pacemaker for regulatory approval and commercialization of AVIM therapy-enabled commercial devices.

Medtronic is the global market leader in cardiac rhythm management ("CRM"), and pacemaker devices, with over 50% of the U.S. market share for such devices and typically having a leading share in all other global markets. Given Medtronic's market leadership and the potential therapeutic benefits of BackBeat CNT, we believe BackBeat CNT-enabled pacemakers, if commercially approved, have the potential to be rapidly adopted into existing pacemaker-indicated patient care for addressable hypertensive patients. We further believe the substantial potential added clinical value and differentiation of BackBeat CNT-enabled pacemakers can help Medtronic potentially expand market share and grow revenue.

Under the terms of the Medtronic Agreement, Medtronic will have exclusive rights in the Primary Field to commercialize BackBeat CNT-enabled pacing systems globally following receipt of regulatory approvals. Medtronic would be entirely responsible

for global commercialization following any receipt of regulatory approvals, including manufacturing, sales, marketing and distribution costs.

Under the terms of the Medtronic Agreement, we are expected to receive between $500 and $1,600 per BackBeat CNT-enabled device sold based on a formula of the higher of (1) a fixed dollar amount per BackBeat CNT-enabled device (amount varies materially on a country-by-country basis) or (2) a percentage of the BackBeat CNT generated sales. This estimated range is derived from publicly-available information, our management's knowledge of the pacemaker market, our discussions with Medtronic, and the terms of the Medtronic Agreement. Based on our discussions with Medtronic, the global market leader in pacemakers, the terms of the Medtronic Agreement and our management's knowledge of reimbursement codes for medical devices, we believe that BackBeat CNT-enabled pacemakers can be supported by existing reimbursement codes without the need for new codes.

Under the terms of the Medtronic Agreement, Medtronic has a right of first negotiation through FDA approval of BackBeat CNT for the Primary Field, to expand its global rights to BackBeat CNT for the treatment of HTN patients not indicated for a pacemaker (the "Secondary Field").

In addition to customary early termination provisions, the Medtronic Agreement will terminate on the date no further revenue share payments are due under the Medtronic Agreement and Medtronic's license under the Medtronic Agreement would become fully paid up, perpetual, irrevocable and royalty-free. Revenue share payments with respect to each applicable country (or group of countries) are to be paid for a minimum period of time determined by the latest to occur of (a) the expiration of the last valid claim of certain specified patents or (b) the date that is 12 years after the first commercial sale of any Backbeat CNT-enabled pacemakers in the applicable country or group of countries.

Market Needs

Hypertension

HTN is elevated blood pressure that increases risk of major cardiac events like heart attack and stroke and can contribute to other significant conditions such as heart failure and kidney disease. HTN is the leading global risk factor for death according to the WHO. An estimated 1.28 billion adults have HTN worldwide according to the WHO.

In the United States, 122.4 million adults, or approximately 47% of all adults, are estimated to have HTN according to the AHA. The AHA and the American College of Cardiology ("ACC") established new *Hypertension Clinical Practice Guidelines* in 2017. According to these guidelines, Stage 1 hypertension is defined for patients with systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg. Stage 2 hypertension now encompasses patients with a systolic BP of at least 140 mmHg or a diastolic BP of at least 90 mmHg. These updated guidelines increased the number of patients believed to have HTN to approximately 47% of all adults from 31.9% under prior guidelines. Global guidelines have yet to be updated to be in line with U.S. clinical practice and generally HTN diagnosis starting at blood pressure at the level of U.S. Stage 2 HTN or above 140 mmHg for systolic BP. Importantly, 77% of U.S. adults over age 65, the age group most likely to need pacemakers, now have HTN according to the new guidelines. Further, the guidelines also recommend that a substantial proportion of U.S. adults taking antihypertensive medication undergo a more intensive BP lowering treatment to get their HTN under control.

High blood pressure was a primary or contributing cause of death in 2021 for more than 691,000 people in the United States, nearly 1,850 deaths each day, according to the CDC. By 2035, the estimated direct cost of high blood pressure could increase to $220.9 billion (annual average), according to the AHA. Cardiovascular risk doubles for every 10 mmHg increase in office systolic blood pressure and the mortality rate doubles with an increase of 20 mmHg in office systolic blood pressure, according to the National Center for Biotechnology Information ("NCBI").

Of U.S. patients aware of their HTN diagnosis, about 76% are believed to be taking antihypertensive medication, but only 52% of those have their condition controlled, according to the *Journal of Clinical Hypertension*. Therefore, approximately 60% of hypertensive U.S. adults have uncontrolled HTN. Non-adherence to antihypertensive treatment is a critical contributor to suboptimal blood pressure control and another important risk factor for adverse cardiovascular disease outcomes. An estimated 45% of HTN patients are non-adherent to medications, according to the journal *Medicine.* Thus, many medically responsive patients have high blood pressure simply because they do not take their medications and medication non-compliance is one of the biggest challenges of HTN treatment. In addition, since HTN patients are typically older, they are more likely to use multiple medications for HTN and

other medical conditions: polypharmacy (multiple medications) has been shown to be associated with increased risk of adverse events (fall injury, heart failure, etc.), polypharmacy mismanagement, and drug-drug interactions. Furthermore, AHA estimates as much as 15% of the prevalent HTN population is resistant to medical therapy (“Resistant HTN”), and these patients are 47% more likely to suffer the combined outcomes of death, myocardial infarction, heart failure, stroke, or chronic kidney disease over the median 3.8 years of follow-up than other HTN patients. Because of the factors mentioned above, there is a significant need for alternative therapies to treat HTN, particularly, device-based therapies.

Isolated Systolic Hypertension & Pulse Pressure

Based on data from the National Health and Nutrition Examination Survey III, 74.5% of U.S. adults over 60 years old have HTN, with over 65% of them suffering from isolated systolic hypertension (“ISH”). ISH patients have elevated systolic blood pressure (>140 mmHg), while their diastolic blood pressure remains normal or low (≤90 mmHg). ISH is a more difficult to treat form of HTN because antihypertensive medications generally impact both systolic and diastolic pressure. It is estimated that over 80% of medical treatment failure patients over 60 years old have ISH. ISH patients experience elevated Pulse Pressure (the difference between systolic and diastolic pressures), which is a known significant, independent risk factor for coronary heart disease. According to published literature, a 10 mmHg increase in Pulse Pressure is associated with a 32% increase in risk of heart failure and a 24% increase in risk of stroke (after controlling for systolic BP and other risk factors). In addition, in men ≥60 years old (which happens to be the typical age of pacemaker patients), risk for coronary artery disease is three times larger in patients with Pulse Pressure of ≥70 mmHg compared to those with Pulse Pressure of 60 mmHg.

Hypertension among Patients with Pacemakers

Pacemakers are recommended for the management of symptomatic bradycardia (slow heart rate) due to sick sinus syndrome, atrio-ventricular block, a combination of these conditions or other situations in which patients are prone to brady-arrhythmias. Currently available devices have evolved from single-chamber, fixed-rate pacemakers to multi-chamber, rate-responsive units. Over 80% of pacemaker patients receive dual-chamber devices which have wires or leads implanted in the right atrium and right ventricle of the heart capable of sensing and stimulating the heart to control contraction timing of both chambers. There were nearly 1.1 million pacemaker implants performed worldwide in 2021, including an estimated 427,500 in the United States according to LSI & HRI Research. Global sales of pacemakers exceeded $4.5 billion in 2022 according to GlobalData, comprising 25% of the overall $18.0 billion market for implantable cardiac rhythm management devices.

Based on the new ACC/AHA guidelines, we estimate that nearly 80% of U.S. patients that are indicated for the implant of a pacemaker have HTN. Among this group of patients, over 60% are estimated to have uncontrolled HTN based on the treatment goal per the 2017 ACC/AHA guidelines. Further, since the average age of pacemaker-indicated patients is approximately 73 years old and, in consideration of other demographic factors associated with this population, these patients are at elevated risk of ISH (over 80% of patients enrolled in prior clinical studies of BackBeat CNT had ISH). Furthermore, these patients are likely to suffer from other co-morbidities common to this population such as atherosclerosis, hyperlipidemia, diabetes mellitus and chronic kidney disease. We believe these patients could benefit substantially from a HTN therapy like BackBeat CNT that can be administered via an already necessary pacemaker.

Target Patient Populations and Market Opportunity for AVIM Therapy

The initial target market for AVIM therapy (BackBeat CNT) is the large population of patients with uncontrolled HTN who also require the implant or replacement of a pacemaker (the HTN+P population). Pursuing this patient population takes advantage of the fact that AVIM therapy is designed to address patients who already require a pacemaker implant since it can be readily incorporated into standard cardiac rhythm management systems such as pacemakers, as Medtronic has already done for the BACKBEAT pivotal study. As a novel HTN therapy completely integrated with an established existing commercially-available device patients already require for a critical medical indication, we believe AVIM therapy can be readily adopted into the existing paradigm of care for hypertensive patients that already require a pacemaker implant. As already described above, we believe there is a significant unmet need and commercial opportunity for more effective treatment of the HTN+P population.

AVIM therapy-enabled pacemakers can be implanted using standard implant procedures, electrical leads and lead positions. Further, we believe any experienced and trained physicians who perform pacemaker implants, such as electrophysiologists and cardiologists, will be able to select a AVIM therapy-enabled pacemaker for an appropriate patient without the need for another

physician referral, if approved. AVIM therapy features proprietary algorithms that are designed to enable physicians to non-invasively adjust the therapeutic parameters to optimize chronic blood pressure reduction to individual patient needs. In addition, AVIM therapy is designed to be de-activated or reactivated by the physician as necessary, offering potential efficacy and safety advantages over other device-based therapies. Importantly, the therapeutic effects of AVIM therapy are designed to not rely on patient adherence or compliance, offering a significant complement to pharmaceutical therapies for which adherence and compliance are a key challenge.

We estimate that the addressable annual market for pacemaker-indicated patients with HTN will comprise more than 750,000 patients worldwide by 2025. We estimate that, if approved, commercialization of BackBeat CNT in hypertensive pacemaker patients can increase the commercial value of the global pacemaker device market by over $2 billion annually. This substantial annual opportunity is based on incorporating BackBeat CNT's potentially potent and clinically impactful HTN treatment capabilities into a pacemaker to drive a meaningful increase in the average selling price ("ASP") that can be supported by existing pacemaker procedure codes globally.

We also believe BackBeat CNT may offer therapeutic benefit to select high-risk HTN patients not indicated for a pacemaker who have uncontrolled systolic blood pressure despite medical therapy and have elevated risk factors such as ISH and additional serious medical comorbidities. We estimate that this additional addressable annual market for high-risk HTN patients will comprise at least 2.4 million patients worldwide by 2025, or approximately 0.2% of the global HTN population. We calculate this estimated market using information from publicly available third-party sources and only includes those hypertensive patients who are (1) of similar age as the pacemaker-indicated patient population (~73 years old on average), (2) have ISH, (3) have high systolic blood pressure (greater than 150 mmHg oSBP) despite medical therapy, and (4) have at least one major co-morbidity (such as artery disease, diabetes, kidney disease, etc.). Using similar maximum ASP figures based on existing reimbursement codes for pacemaker implantation, we estimate that this calculated market represents a global potential annual revenue opportunity of over $8 billion using similar potential ASPs as BackBeat CNT-enabled pacemakers.

Impact Potential of BackBeat CNT

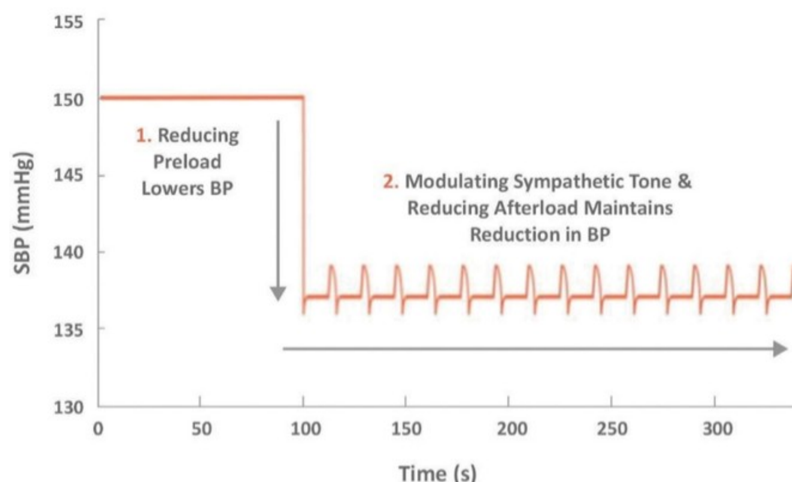
BackBeat CNT, also known as AVIM therapy, is a bioelectronic product candidate for HTN that is designed to substantially reduce blood pressure. BackBeat CNT is delivered through programmed cardiac pacing algorithms. These algorithms are specifically designed to reduce blood pressure by (1) lowering cardiac preload (ventricular filling volume) and maintaining reduced blood pressure and by (2) modulating sympathetic tone (the level of activity of the sympathetic nervous system) as well as reducing cardiac afterload (total peripheral resistance). AVIM therapy is designed to leverage standard rhythm management devices (dual-chamber pacemaker), utilizing the same implant procedure and lead positions while still enabling standard rhythm management (pacing) functions. We believe that physicians such as implanting cardiologists and electrophysiologists who currently implant pacemakers and are responsible for the care of these patients can make the medical decision to implant a AVIM therapy-enabled pacemaker in an eligible patient. Further, we believe that AVIM therapy-enabled devices can garner meaningfully higher ASPs that can be supported by existing reimbursement without the need for new procedure codes. While AVIM therapy is designed to achieve certain results as described above and below, there is no guarantee that AVIM therapy will prove to be safe and effective.

AVIM therapy is designed to deliver cardiac pacing to reduce blood pressure through two essential mechanisms:

1. Programmed pacing with short atrial-ventricular ("AV") delays (shorter timeframe between contraction of the atria and the ventricle of the heart) designed to substantially reduce blood pressure by reducing cardiac preload. Cardiac preload is the amount of stretching of the ventricle of the heart driven by the volume of blood that fills the ventricle. Pacing with shorter AV delays reduces fill volume and, thereby, cardiac preload. Lower preload results in lower blood pressure.

2. Programmed variable blood pressure patterns (achieved using programmed pacing with a combination of shorter and longer AV delays) designed to maintain average blood pressure reduction by modulating sympathetic tone and reducing cardiac afterload. Sympathetic tone refers to the level of activity of the sympathetic nervous system response which is known to drive

and maintain elevated blood pressures. Cardiac afterload is the vascular resistance against which the heart has to contract to eject blood and is characterized by the diameter of arteries, otherwise known as total peripheral resistance.



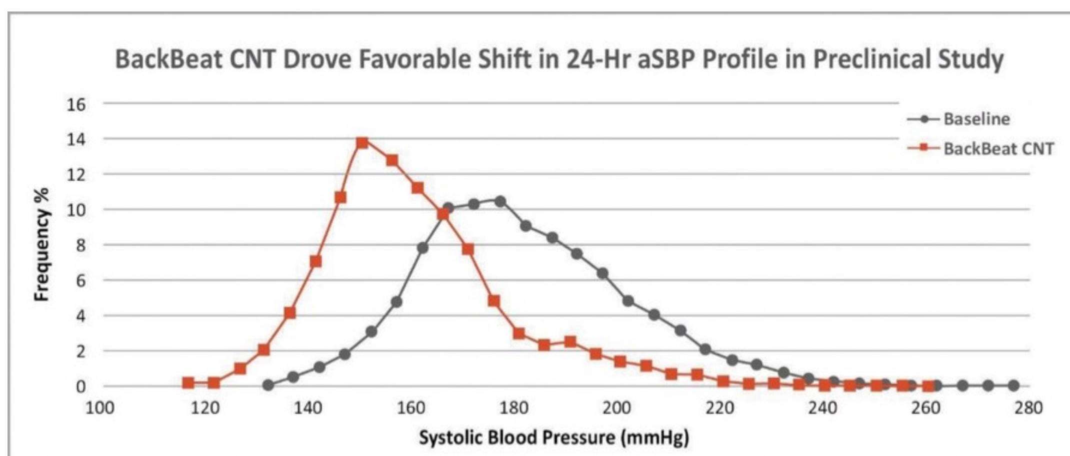
Preclinical Data

The goal of the preclinical studies was to evaluate the feasibility of the use of BackBeat CNT in a canine model with surgically induced HTN and to provide a rationale for clinical use to persistently lower blood pressure in patients with HTN. BackBeat CNT was delivered via pacing algorithms in a prototype device in the canine model. Chronic delivery of BackBeat CNT significantly reduced 24-hour aSBP by an average of 32.5 mmHg over a one-month period (n=4).

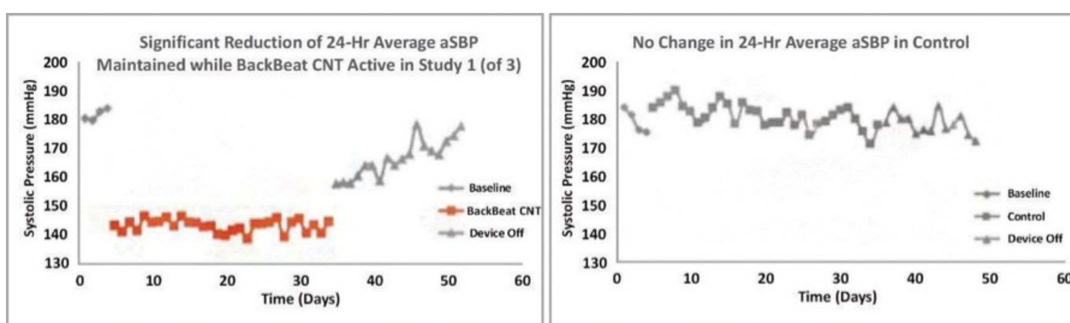
The reduction occurred immediately upon activation of therapy and was maintained for the period that the therapy was active (approximately 30 days). Blood pressure did not meaningfully change in the study's single control animal that had a BackBeat CNT device implanted, but not activated. 24-hour aSBP was measured using an implanted blood pressure sensor.

The chart below shows the baseline 24-hour aSBP profile of one of the study animals prior to therapy activation as compared to the 24-hour aSBP profile of the same animal following activation of BackBeat CNT. The results are plotted as a histogram demonstrating the frequency of blood pressure levels over the course of the 24-hour period. The baseline aSBP histogram shows the percentage frequency of aSBP reaching different levels of pressure ranging from approximately 135 mmHg to 280 mmHg and a most frequent aSBP of approximately 180 mmHg. By contrast, the BackBeat CNT aSBP histogram shows the percentage frequency of aSBP reaching different levels of pressure ranging from approximately 120 mmHg to 260 mmHg and a most frequent aSBP of approximately 145 mmHg. The charts demonstrates the significant improvement in the entire 24-hour aSBP profile of the animal driven by BackBeat CNT as the entire aSBP histogram is shifted substantially downwards and to the left in term of frequency of reaching lower SBP levels and the peak SBP frequency level is reduced by approximately 35 mmHg. These results are similar in the

three BackBeat CNT study animals in terms of substantial improvement of the 24-hour aSBP profile while the one study control animal did not experience a shift in 24-hour aSBP profile.



The chart below on the left shows average aSBP per 24-hour period of the same study animal profiled above over the entire study period. This chart demonstrates that (1) BackBeat CNT drove a substantial reduction of 24-hour aSBP from baseline levels (shown in orange with each box representing a full 24-hour period of aSBP measurement); (2) this blood pressure reduction was maintained through the period that BackBeat CNT was active (as reflected in the orange line made up of orange boxes); and (3) blood pressure levels took more than 10 days to return to baseline levels after BackBeat CNT was turned off, indicating that sympathetic tone responses and afterload levels were potentially modulated by chronic delivery of BackBeat CNT since aSBP levels would be expected to return immediately to baseline levels if sympathetic tone and afterload were not modulated. These results are similar in all three BackBeat CNT study animals in terms of durable substantial improvement of the 24-hour aSBP profile and slow response over days to baseline aSBP levels. As shown in the chart below on the right, the one study control animal did not experience any significant changes in 24-hour aSBP during the study period as illustrated by the chart below.



Clinical Results

Acute Clinical Study:

A short time-based study of the effects of the BackBeat CNT therapy in 18 patients with HTN who were already scheduled to undergo an invasive electrophysiology procedure was conducted at Jiangsu Province Hospital/The First Affiliated Hospital with Nanjing Medical University, Nanjing, China. The study population consisted of patients with HTN and systolic blood pressure >140 mmHg despite at least one antihypertensive medication.

BackBeat CNT was applied for at least one minute in all patients and up to five minutes in certain patients based on whether the physician managing the primary electrophysiology procedure allowed for longer duration of treatment based on the time available to perform the BackBeat CNT acute clinical study versus the primary electrophysiology procedure for which the patient was being treated. Various signal parameters were evaluated. All patients exhibited reduction of >10 mmHg in systolic blood pressure. The average sustained reduction in blood pressure was 19.7 +/-7.4 mmHg systolic (p<0.001) and 4.3 +/-3.7 mmHg diastolic (p<0.001). No serious adverse effects were observed or reported in these studies. The study also demonstrated that reduction in blood pressure was titrated by modifying BackBeat CNT parameters as needed.

Chronic Clinical Studies:

MODERATO I Single Arm Study

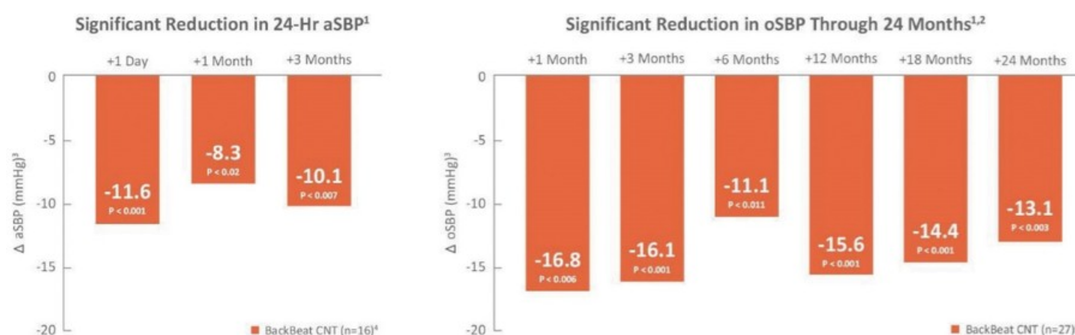
The 27-patient, MODERATO I clinical study was conducted in Europe and Chile to evaluate the safety and efficacy of BackBeat CNT therapy using our proprietary Moderato system, capable of delivering BackBeat CNT as well as performing the rhythm management function of a standard dual-chamber pacemaker. The Moderato system, comprised of the IPG and programmer, was manufactured under an original equipment manufacturer ("OEM") contract by a division of Integer Holdings Corporation ("Integer"), a leading supplier of cardiac rhythm management device components. The Moderato system was CE marked in July 2019. However, we do not plan to commercialize the Moderato device but may consider utilizing the CE marked system to conduct additional clinical work in the EU.

The results from the MODERATO I study were published in December 2017 in the *Journal of the American Heart Association*. The main inclusion criteria required patients to have oSBP >150 mmHg despite taking at least two anti-hypertensive drugs as well as having a clinical indication for a dual-chamber pacemaker implant or replacement. Twenty-seven patients meeting all study entry criteria underwent a Moderato device implant, at which time only standard pacemaker functions were activated. Nearly 80% of the patients enrolled had ISH, making them a more difficult group of patients to treat. All enrolled patients were implanted with Moderato devices and then followed for a one-month observation period to evaluate any changes in blood pressure due to either the initiation of standard pacing alone or due to their participation in the study. At the end of the one-month period blood pressure was reassessed to ensure oSBP remained >140 mmHg for eligibility to enter the treatment phase of the study. Only 27 patients met the criteria and in these patients BackBeat CNT was activated. Patients were then reevaluated following three months of treatment for changes in blood pressure assessed by both office cuff measurements and by 24-hour ambulatory blood pressure recordings. The study's co-primary efficacy endpoints were changes in oSBP and mean 24-hour aSBP (added as study amendment) from pre-activation through three months post activation of therapy. All 27 patients completed the study's three-month activation period and clinical follow-up. Twenty-one patients consented to be followed at 6, 12, 18 and 24 months after activation and only oSBP levels were measured at these longer follow-up time points due to the fact that measuring changes in aSBP over two- to six-month periods is generally deemed appropriate to asses HTN therapies and because additional aSBP measurements are highly burdensome for patients that participate in HTN studies as they require wearing a device that takes frequent blood pressure measurements over a 24-hour period. Two-year follow-up data available from these 21 patients was presented for the first time in October 2017 at the Transcatheter Cardiovascular Therapeutics (TCT) conference in Denver, Colorado.

The co-primary efficacy endpoint of changes in mean 24-hour aSBP was met successfully with BackBeat CNT activation driving a significant 11.6 mmHg reduction (p<0.001) from pre-activation levels during the first day of therapy. The reduction was maintained through the three-month activation period, representing a statistically significant reduction of 10.1 mmHg (p=0.007) from the pre-activation aSBP. Seventeen of the 27 study patients participated in the co-primary efficacy endpoint analysis which was included as amendment to the MODERATO I study design following initiation of the study given new evidence from other clinical studies regarding the potential importance of change in mean 24-hour aSBP in assessing the potential efficacy of HTN therapies.

The co-primary efficacy endpoint of changes in oSBP was also met successfully with BackBeat CNT driving a statistically significant reduction in oSBP, 16.1 mmHg (p<0.001) from pre-activation levels. This reduction in oSBP was maintained in patients

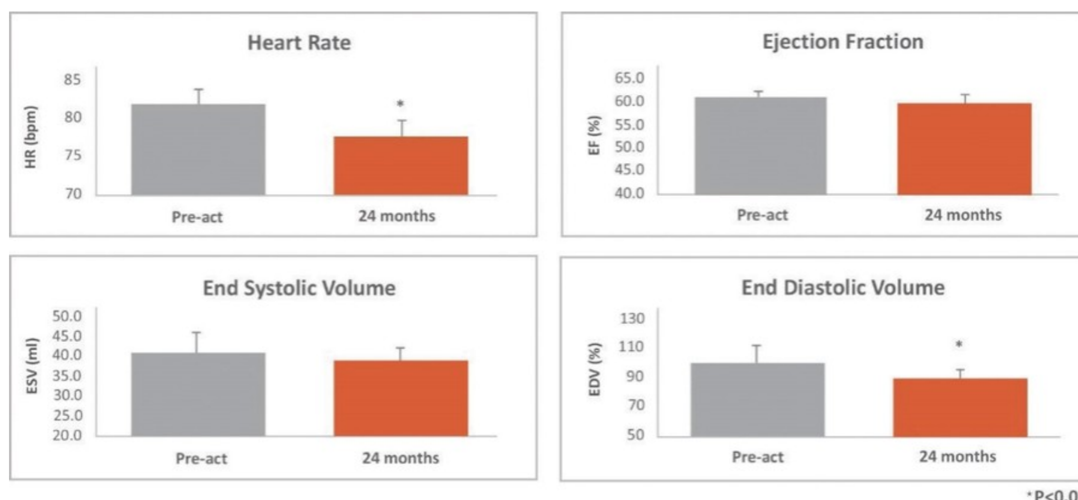
who reached the later follow-up time points with a mean statistically significant reduction of 23.4 mmHg ($p<0.001$) in oSBP from baseline levels after 24 months of therapy.



[1]Neuzil et al. Journal of the American Heart Association. 2017;6:e006974. https://doi.org/10.1161/JAHA.117.006974. [2]Burkhoff MODERATO I Study 2-Year Results TCT 2018.
[3]Compared to pre-activation. [4]16 patients had aSBP at pre-activation. [5]21 of 27 patients continued after completion of study at 3 months to be followed for 2 years

Long-term (24-month) data showed results consistent with expected mechanism of action, including statistically significant reduction in heart rate ($p<0.05$), a key measure of sympathetic nervous system activation, and end-diastolic volume, a key safety measure. In addition, comparison of echocardiograms performed at baseline and following activation up to two years of BackBeat CNT therapy showed that there were no significant changes in cardiac function (ejection fraction).

24-month Data Consistent with Expected Mechanism of Action



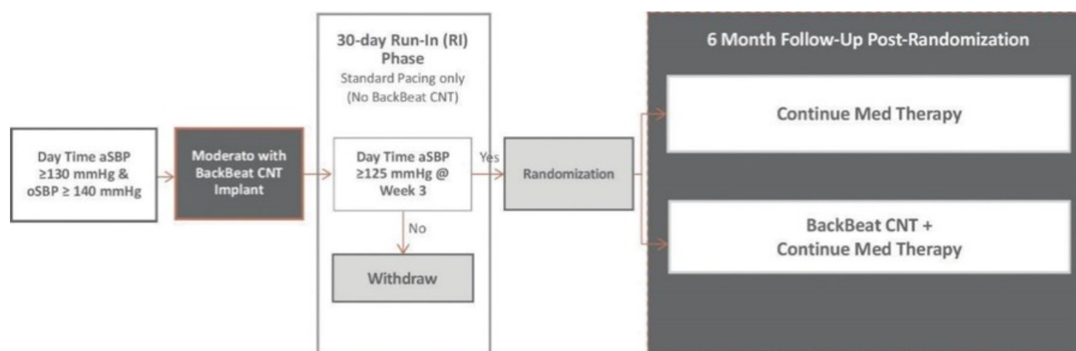
During the initial study period for MODERATO I, there were eleven SAEs in seven of the 27 study patients. Nine events in six patients were cardiac related. Two non-cardiac events were urinary tract infection and dyspnea treated with bronchodilator. No events were adjudicated as definitely or probably related to BackBeat CNT. One event was adjudicated as probably related to the implant procedure for the Moderato device. Four events in four patients were adjudicated as possibly related to the Moderato device (atrial fibrillation, myocardial infarction with symptoms of heart failure, cardiac asthma, and arrhythmia due to ventricular oversensing).

During the extended 21-month follow-up period that included 24 patients who continued with BackBeat CNT, there were 25 SAEs in twelve patients. No events were adjudicated as definitely or probably related to BackBeat CNT. Out of 25 events, 17 events

in seven patients were cardiac related. There were eight non-cardiac events in eight patients. The non-cardiac events included two orthopedic events, two cases of cancer, a transient ischemic event, and three respiratory related events. Five events in three patients were adjudicated as possibly device related. These included two events of atrial fibrillation in the same patient, pneumonia with cardiac decompensation and dyspnea with cardiac decompensation in one patient, and cardiac decompensation in another patient.

MODERATO II Double-Blind, Randomized Study

The results of the MODERATO II study of BackBeat CNT in hypertensive patients also indicated for a pacemaker were published in August 2021 in *the Journal of the American Heart Association*. All patients enrolled in the MODERATO II, a European prospective, multi-center, double-blind, randomized pilot study of BackBeat CNT, had persistent HTN (aSBP ≥ 130 mmHg and oSBP ≥ 140 mmHg) despite one or more anti-hypertensive medications and a pacemaker indication, and were implanted with our Moderato System. Following a 30-day run-in period during which patients received only standard pacing along with anti-hypertensive medications, patients who met follow-up screening criteria for daytime aSBP were randomized to BackBeat CNT or control groups.



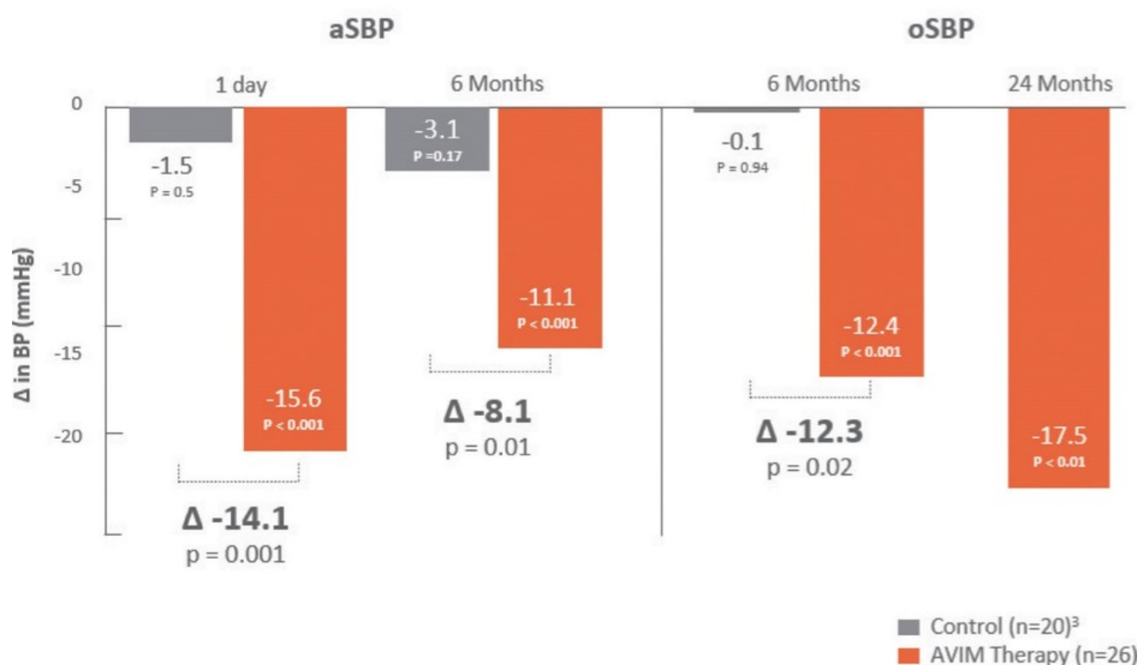
Prior to randomization, mean aSBP for both groups was 136.3 mmHg with patients, on average, treated with over three prescribed anti-hypertensive drugs. 88.5% of the patients in the BackBeat CNT treatment arm had ISH, making them a more challenging group of patients to treat. 71.4% of control arm patients also had ISH. The study met its primary efficacy endpoint of superiority of BackBeat CNT to control in terms of change in mean 24-hour aSBP at six months following randomization. After six months, mean aSBP was reduced by a statistically significant 11.1 mmHg in the BackBeat CNT group as compared to a non-significant reduction of 3.1 mmHg in the control group, resulting in a statistically significant difference of 8.1 mmHg (p=0.01) between groups.

The treatment group saw a high (85%) overall response rate, with approximately 54% of the BackBeat CNT-treated patients experiencing aSBP reduction at six months of greater than 10 mmHg, an amount associated with a clinically meaningful reduction in risk of heart attack and stroke.

The study met its secondary efficacy endpoint of superiority of BackBeat CNT to control in terms of change in oSBP at six months following randomization. After six months, oSBP was reduced by a statistically significant 12.4 mmHg in the BackBeat CNT group as compared to a non-significant reduction of 0.1 mmHg in the control group, resulting in a statistically significant difference of 12.3 mmHg (p=0.02) between groups.

The MODERATO II study also met its primary safety endpoint, which was no significant differences in rates of MACE. There were no MACE in the BackBeat CNT group and three MACE in two patients in the control group (one death from cancer and two cardiac events) at six months. Additionally, there were no notable differences in echo parameters between the two arms. During the randomized phase of the study, there were eight SAEs in four patients in the control group (n=21) and none in the treatment group (n=26). Two of the eight events were cardiac related. During the extended 18-month follow-up period that included treatment patients (n=26) and crossover-to-treatment patients (n=14), there were 26 SAEs in 16 patients. Out of 26 events, only 13 events (in eleven patients) were cardiac related. No events were adjudicated as possibly related to BackBeat CNT. The non-cardiac events included four cancer related events, for gastrointestinal disorder events, one COVID-19 death, one amputation, two inflammatory events, and a transient ischemic event.

BackBeat CNT-treated patients in the MODERATO II study continued to be followed through the 24-month period of the study, including control patients who crossed over to BackBeat CNT after the end of the six-month double-blind period of the study. Only oSBP measurements were taken at follow-up visits after the six-month aSBP primary endpoint was measured. Significant reduction in oSBP, a mean of 17.5 mmHg, was maintained in all BackBeat CNT-treated patients who completed the 24-month follow-up. The results for 24-hour aSBP and oSBP at six months post-randomization, as well as the oSBP results at 24 months are shown in the figure below:



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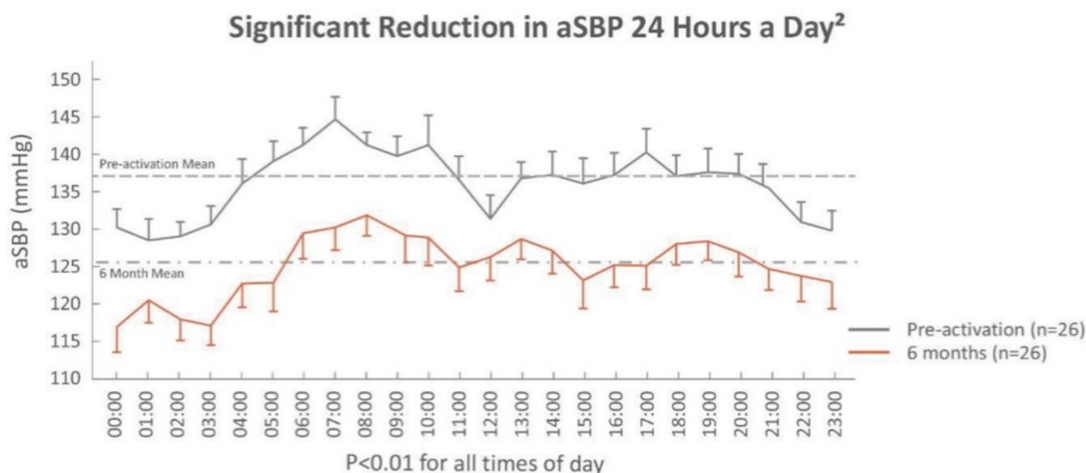
(1) Kalaras et al. Journal of the American Heart Association. 2021;10:e020492 ahajournals.org/doi/10.1161/JAHA.120.020492;

(2) Burkhoff MODERATO II Study 2-Year Results TCT 2021;

(3) 24-Hr aSBP Control (n=19), 1 control patient could not be measured despite repeat measurement (patient had extremely high blood pressure);

Definitions: Major Adverse Cardiac Events (MACE) included death, heart failure, clinically significant arrhythmias (i.e., persistent or increased atrial fibrillation, serious ventricular arrhythmias), myocardial infarction, stroke and renal failure in treatment group calculated per patient; Office Systolic Blood Pressure (oSBP); and Ambulatory Systolic Blood Pressure (aSBP).

Additionally, as shown in the chart below, the mean 24-hour aSBP profile (systolic blood pressure plotted over a 24-hour period) for all 26 BackBeat CNT patients pre-activation (prior to BackBeat CNT) was significantly reduced at six months following BackBeat CNT activation at all time points.



Following completion of the randomized period and successful achievement of the primary endpoints, 14 control patients crossed over to active BackBeat CNT. Nine of the fourteen patients had ISH. The results in these patients were encouraging and consistent with the reductions in the BackBeat CNT group during the randomized portion of the study and are summarized below:

- Statistically significant mean reductions in aSBP (-10.3±9.3 mm Hg, p<0.01) and ambulatory pulse pressure (-11.7±5.5 mmHg, p<0.01) at six months post therapy activation compared to pre-crossover.

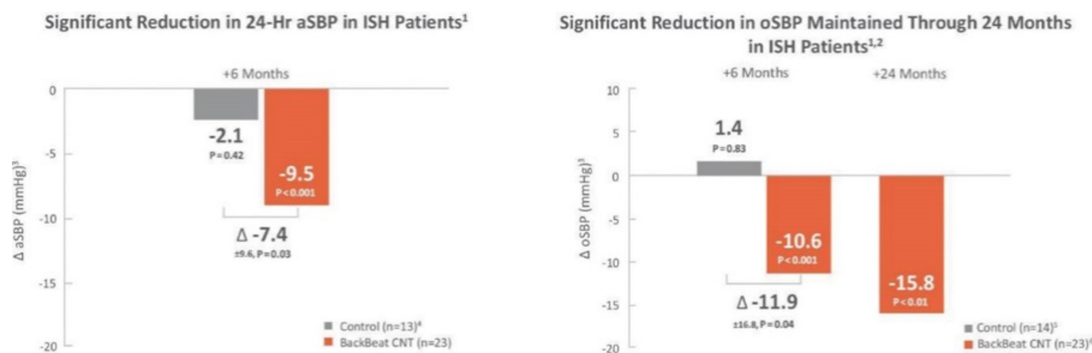
- Minimal changes in mean ambulatory diastolic blood pressure (+1.5±5.5 mmHg, p=NS) at six months post therapy activation compared to pre-crossover.

- Mean oSBP decreased by 13.1±26.6 and 13.8±28.7 mmHg at six and eighteen months post therapy activation, respectively, compared to pre-crossover.

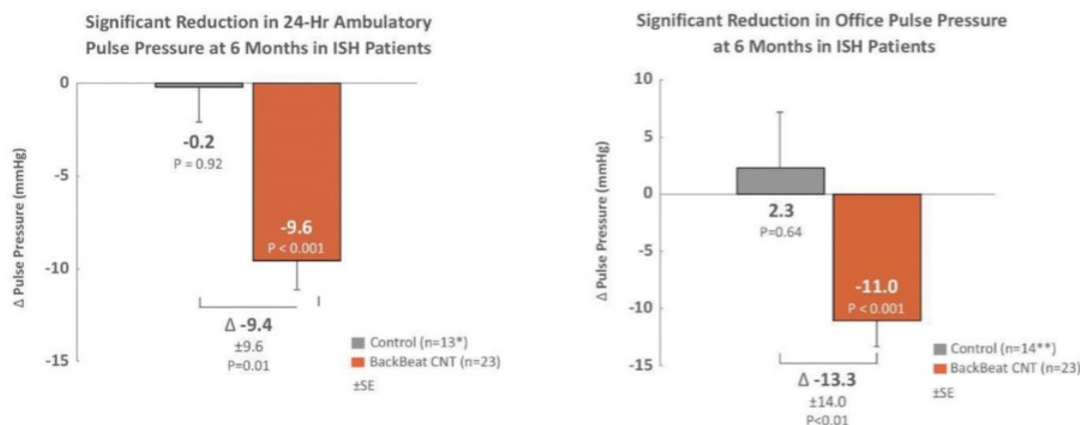
BackBeat CNT in Patients with ISH

In a subgroup of patients with ISH, a dangerous and challenging to treat form of HTN prevalent in older patients, treatment with BackBeat CNT resulted in clinically meaningful and statistically significant reductions of 7.4 mmHg in aSBP and 11.9 mmHg in oSBP when compared to control (continued medical therapy) patients at six months. Further, in patients with ISH, BackBeat CNT

drove statistically significant reductions of 9.4 mmHg in ambulatory Pulse Pressure and 13.3 mmHg in office Pulse Pressure at six months as compared to control patients.



[1]Kalaras et al. Journal of the American Heart Association. 2021;10:e020492. https://doi.org/10.1161/JAHA.120.020492. [2]Burkhoff MODERATO II Study 2-Year Results TCT 2021. [3]Compared to pre-activation. [4]13 control patients at 6 months, one died of cancer, and one had unsuccessful recording. [5]14 control patients at 6 months, one died of caner. [6]21 patients at 24 months, one died of cancer, and one died from Covid-19



*13 control patients at 6 months, one died of cancer, and one had unsuccessful recording
**14 control patients at 6 months, one died of cancer

Our Approach to Supporting Clinical Studies to Date

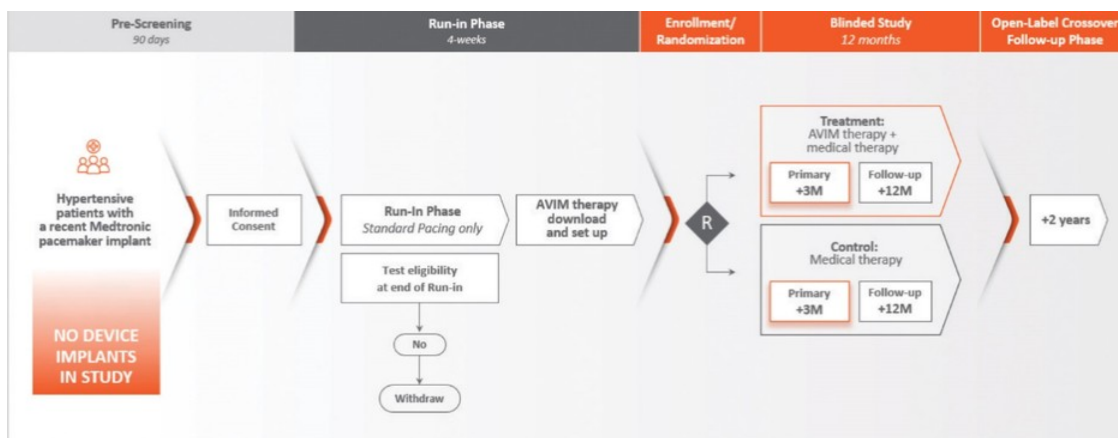
We utilize a four-pronged approach to support clinical activities for BackBeat CNT: (1) full-time employees to directly manage clinical studies and supervise external providers; (2) an external CRO, that serves as the authorized and legal representative of the study sponsor, submits study protocol for approval by clinical site review boards and ethics committees, and reports adverse events; (3) local part-time independent clinical research associates (“CRAs”), in the countries in which BackBeat CNT studies have clinical research sites that are responsible for the site initiation and full data monitoring; and (4) field clinical technical support and patient enrollment personnel that are independent contractors working under consulting agreements.

Regulatory and Commercialization Pathway

We plan to conduct a global pivotal clinical study in collaboration with Medtronic to support potential FDA, EU, Japanese and other global regulatory approvals of AVIM therapy for the treatment of hypertension in patients who are indicated for a pacemaker. This study is called the BACKBEAT (**B**radyc**A**rdia pa**C**ema**K**er with atrioventricular interval modulation for **B**lood pr**E**ssure tre**A**tmen**T**) pivotal study. On September 19, 2023, we announced that the FDA granted us IDE approval to initiate our planned

BACKBEAT pivotal study of AVIM therapy (BackBeat CNT) to treat hypertension in patients indicated for a pacemaker. We currently expect to initiate enrollment of the BACKBEAT pivotal study before the end of 2023 following completion of clinical trial initiation activities, including clinical center Institutional Review Board approvals.

The BACKBEAT pivotal study is a global, multi-center, prospective, randomized, double-blind study investigating the efficacy and safety of AVIM therapy in patients who recently underwent a Medtronic dual-chamber cardiac pacemaker implant and have uncontrolled hypertension (“HTN”) despite the use of antihypertensive medications. The study will randomize approximately 500 participants 1:1 to AVIM along with continued medical therapy and pacing (treatment) or continued medical therapy and pacing alone (control). The study’s primary efficacy endpoint is superiority of treatment as compared to control based on mean change in 24-hour ambulatory systolic blood pressure (aSBP) at three months post randomization. The primary safety endpoint is freedom from unanticipated serious adverse device effects in the treatment arm at three months post-randomization. Double-blind follow-up will continue through 12 months to enable collection of additional clinical endpoints. The BACKBEAT pivotal study will enroll patients in as many as 80 clinical sites worldwide and we expect to begin enrollment in the BACKBEAT pivotal study before the end of 2023. We expect to utilize a similar overall approach to execution of the BACKBEAT pivotal study that we have used for prior clinical studies with the added benefit that we will be able to utilize expert field clinical support from Medtronic for certain aspects of study support activities.



In the third quarter of 2019, the Moderato implantable system that delivers BackBeat CNT for the treatment of HTN while also providing standard pacemaker functions was CE marked in the EU under the Active Implantable Medical Device Directive. We currently do not have plans to commercialize this system in the EU on our own but believe there is a significant opportunity for Medtronic to commercialize AVIM therapy-enabled pacemakers in the EU post-marketing approval. The BACKBEAT pivotal study will include at least 20 clinical study sites in the EU, including several sites that participated in the MODERATO I and II studies.

For the clinical and regulatory development of AVIM therapy for High-Risk HTN, we will seek to leverage data from the BACKBEAT pivotal study given that age and other demographic factors of the target population are expected to be similar, the type of hypertension treated will likely be isolated systolic hypertension which is a predominant form of HTN in the HTN+P population, and other comorbidities are also expected to be similar to both target populations.

CNT-HF for Heart Failure

Our Bioelectronic Therapies group is also seeking to develop a pipeline of additional treatments for development and future licensing based on its patented CNT technology. The lead follow-on therapy candidate is CNT-HF, a bioelectronic treatment for HF. According to the AME Medical Journal, HF affects an estimated 64 million people worldwide. According to the CDC, 6.8 million Americans have HF, which contributed to 1 in 8 deaths in the United States in 2020, while costing nearly $31.0 billion annually. AHA projects the cost of HF will increase by 127% to $69.8 billion in 2030, amounting to approximately $244 for every U.S. adult. Approximately half of the patients with signs and symptoms of heart failure have largely normal left ventricular ejection fraction and are therefore considered Heart Failure patients with Preserved Ejection Fraction (“HFpEF”), according to the AHA. The prevalence of

HFpEF compared with prevalence of HF with reduced ejection fraction (“HFrEF”), appears to be increasing over time along with aging of the population and the increasing prevalence of risk factors for HFpEF, such as obesity, HTN, and type 2 diabetes as well as improvements in diagnosis, according to the AHA. Those living with HFpEF experience frequent hospitalizations and high mortality rates. Nevertheless, there are currently no approved disease-modifying therapies for HFpEF. The success of existing HF therapies is mostly limited to treatment of HFrEF, not HFpEF, according to GlobalData.

CNT-HF is a modified cardiac neuromodulation therapy algorithm that, like BackBeat CNT, aims to achieve autonomic nervous system modulation with a primary focus on sympathetic down-regulation without substantial impact on blood pressure. HF is a syndrome characterized initially by left ventricular dysfunction that triggers countermeasures aimed to restore cardiac output. These responses are compensatory at first but eventually become part of the disease process itself, leading to further worsening cardiac function. Among these responses is the activation of the sympathetic nervous system (“SNS”), that provides inotropic support to the failing heart increasing stroke volume, and peripheral vasoconstriction to maintain mean arterial perfusion pressure, but eventually accelerates disease progression affecting survival. Activation of SNS has been attributed to the withdrawal of normal restraining influences and the enhancement of excitatory inputs, leading to worsening heart failure symptoms and progression of disease.

In 2021, we initiated an exploratory European acute clinical study of CNT-HF for the treatment of patients with HF. An initial ten patient cohort was treated acutely with an exploratory CNT-HF algorithm. We have analyzed results from this cohort and have proceeded to initiate acute treatment of a second patient cohort using a CNT-HF algorithm that is enhanced based on the results from the first patient cohort. If the results from these acute clinical studies are encouraging, We will seek to initiate a chronic feasibility implant clinical study of CNT-HF in 2024.

If safe and effective, we believe CNT-HF for the treatment of heart failure has the potential to be an attractive therapeutic candidate for licensing and collaboration with strategic partners that have established commercial cardiac rhythm management business. We anticipate that CNT-HF will run on a dual-chamber pacemaker, a three-chamber bi-ventricular pacemaker (also known as a cardiac resynchronization therapy or “CRT” device), as well as, potentially, a combined pacemaker/CRT/defibrillator, allowing potential strategic partners already in the cardiac rhythm management business to provide an entirely new HF treatment leveraging their existing manufacturing and commercialization infrastructure.

FOCAL THERAPIES — Virtue SAB for Artery Disease and SirolimusEFR for Local Inflammation in Multiple Indications

We are developing high impact therapeutic product candidates designed to optimize focal drug delivery during well-established interventional procedures with the objective of improving clinical outcomes and reducing complications. Our flagship product candidate of the Focal Therapies group is the Virtue SAB, a drug/device product candidate that is designed to enable targeted delivery of sirolimus, an approved pharmaceutical agent for preventing restenosis during interventional stent treatment of artery disease, the leading cause of death worldwide. We have a global strategic partnership with Terumo, one of the world’s largest medical device companies, for Virtue SAB. We are also working to develop multiple additional applications of SirolimusEFR, our proprietary, investigational extended focal release formulation of sirolimus used in Virtue SAB. Sirolimus is a widely used anti-proliferative, anti-inflammatory pharmaceutical, which we believe in its unique formulation has the potential for the treatment of local inflammation in target tissues other than coronary and peripheral arteries.

Below is a detailed summary of Virtue SAB and an overview of potential future SirolimusEFR-based programs.

Virtue Sirolimus AngioInfusion Balloon

Virtue SAB is a novel, proprietary drug/device combination product candidate for the treatment of artery disease that is designed to deliver an extended focal release formulation of sirolimus to the vessel wall during balloon angioplasty without the need for balloon coating or a permanent implant. Virtue SAB utilizes two key enabling technologies, our proprietary, investigational formulation of sirolimus, SirolimusEFR, and its patented microporous AngioInfusion Balloon, that work synergistically to optimize the clinical performance of the product candidate. Clinical data from the SABRE trial, a multi-center, prospective, independent core lab-adjudicated pilot clinical study of 50 patients conducted in Europe, has positioned Virtue SAB for a U.S. pivotal clinical study to support potential FDA approval for the treatment of ISR. We will sponsor this study, called the Virtue ISR-US. The aim of this study is to have Virtue SAB be the first approved AngioInfusion Balloon for coronary use in the United States. We believe Virtue SAB has the potential for further evaluation in follow-on clinical indications such as treatment of *de novo* coronary small vessel disease (“SV”), and below-the-knee peripheral disease (“BTK”). Terumo is responsible for executing a global clinical and regulatory development

program focused on SV, BTK and coronary indications, with the exception of the Virtue ISR-US trial, for which we have responsibility.

Strategic Partnership with Terumo

In June 2019, we entered into the Terumo Agreement with Terumo, one of the largest medical device companies in the world, with corporate headquarters in Tokyo, Japan, pursuant to which Terumo secured global commercialization rights for Virtue SAB in coronary and peripheral vascular indications (“Subject Indications”). Under the Terumo Agreement, Terumo made an upfront payment to us of $30.0 million and invested a total of $5.0 million in our last two private equity financings and may potentially make additional future clinical and regulatory milestone payments to us. Further, according to the agreement, which is currently in the process of being renegotiated, it is expected that Terumo will assume financial and execution responsibility for substantially all future clinical and regulatory development, with the exception of the Virtue ISR-US trial, for which we are responsible. Our responsibilities in this regard with respect to the current agreement include completing the development of the product in the United States through premarket approval by the FDA for the ISR indication including (i) manufacturing, testing and packaging the drug required for the clinical trials, (ii) supplying Terumo with information related to the design and manufacture of the delivery device and the technology transfer needed for Terumo to ultimately commence manufacture of the delivery device, and (iii) carrying out regulatory activities related to clinical trials in the United States for the ISR indication. Terumo will also be responsible for device manufacturing, commercial sales, marketing and distribution for Virtue SAB for coronary and peripheral vascular indications globally. The agreement also provides for us to be able to perform research, development, clinical, regulatory, manufacturing and supply activities on behalf of Terumo, if requested, and be reimbursed for such services or paid on a “cost plus” basis for supplies. In addition, we will manufacture, or have manufactured, SirolimusEFR and have exclusive rights to sell it on a per unit basis to Terumo for use in the Virtue SAB product, and Terumo may also request other services from us from time to time.

Pursuant to the Terumo Agreement, we share in all of Terumo’s Virtue SAB revenues during the term of the agreement through future royalties of 10-15% of net sales of Virtue SAB, and additional per unit payments for SirolimusEFR used in Virtue SAB for which we are the sole exclusive supplier. The initial term of the Terumo Agreement expires on the tenth anniversary of the date on which the first PMA is obtained from the FDA for Virtue SAB for ISR, and thereafter automatically extends for five-year periods unless terminated by Terumo. Under the Terumo Agreement, we retain the rights to develop and license technology used in Virtue SAB, including SirolimusEFR, for clinical applications outside of coronary and peripheral vascular intervention.

Under the Terumo Agreement, we were initially eligible for certain milestone payments in the amount of $65 million from Terumo upon completion of certain minimum enrollments in clinical studies, making certain filings and submissions, and obtaining certain regulatory approvals and certifications. Of these milestone payments, $35 million relate to achieving certain milestones by specified target achievement dates. As of the date this prospectus, the target achievement date for two $5 million milestone payments has already passed. In addition, due to delays in our Virtue SAB program resulting from the COVID-19 pandemic, supply chain issues and unexpected changes to regulatory requirements, including increased testing and other activities related to chemistry, manufacturing, and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, the Company is unlikely to be able to complete the remaining time-based milestones by the specified target achievement dates to earn the remaining $25 million in time-based milestone payments pursuant to the Terumo Agreement. Further, Terumo has the right to terminate the agreement, or certain of its obligations thereunder, if certain milestones are not achieved over time.

As previously disclosed, we and Terumo have been negotiating mutually agreeable adjustments to the Terumo Agreement that could serve to restructure milestone payments as well as make other potential material modifications to the Terumo Agreement. Until we gain clarity on the likely outcome of such ongoing negotiations, our current expectation is that the initiation of the Virtue ISR-US pivotal study will be postponed until 2024. If negotiations are not completed to our satisfaction or to the satisfaction of Terumo, clinical study, product development, and commercialization plans for Virtue SAB may continue to be adversely impacted.

Market Needs — Coronary and Peripheral Artery Disease

Artery disease is caused by atherosclerosis, the hardening and narrowing of the arteries due to the build-up of fatty material and plaque that reduces blood flow through the blood vessels supplying the heart muscle (CAD) or limbs (PAD). CAD reduces blood flow and oxygen supply to the heart muscle and can result in angina, heart attack and lead to heart failure and arrhythmias. PAD can

happen in any blood vessel, but it is more common in the legs than the arms and can lead to pain, muscle weakness, wounds and ulcers that are difficult to heal and, eventually, amputation.

According to the World Health Organization (the "WHO"), CAD is the top cause of global death, resulting in over 17.8 million deaths annually worldwide. According to the Centers for Disease Control and Prevention (the "CDC"), CAD was responsible for 695,000 deaths in the United States in 2021. According to the American Heart Association (the "AHA"), about 2 in 10 deaths from CAD happen in adults less than 65 years old. About 18.2 million U.S. adults aged 20 and older have CAD (about 6.7%), according to the CDC. Approximately 8.5 million people over age 40 in the United States have PAD, including up to 20% of individuals older than age 60, according to the CDC.

Interventional Cardiology

Interventional cardiology is a medical specialty that uses minimally invasive transcatheter, percutaneous technologies and techniques to treat artery disease and atherosclerosis. Catheter-based interventions using balloon angioplasty, stents and other technologies are the most common medical procedures used to treat artery disease and related conditions. There were over 6.4 million coronary and over 1.6 million peripheral catheter-based interventional procedures performed worldwide in 2022 according to Global Data & LSI Research. The global market for coronary interventional devices used to treat CAD, such as stent and balloon angioplasty systems, was valued at approximately $16.2 billion in 2022, and the global market for devices used to treat PAD, including angioplasty balloons, drug-coated balloons, stents and atherectomy systems, was valued over $4.7 billion in 2022, according to market research firms LSI Research, Fortune Business Insights, and Global Market Insights.

The Evolution of Available Treatment Options

Balloon angioplasty is a procedure where small balloons integrated into catheters are introduced into the vascular system through a small puncture in the femoral artery in the leg or radial artery in the arm. Using specialized imaging technology called angiography, the balloon catheter is threaded through the vasculature to the site of blockage in an artery in the heart (coronary) or in the peripheral vessels. The balloon is then inflated using high pressures (up to 20 atmospheres) in order to crush the blockage (plaque) and expand the artery to restore blood flow.

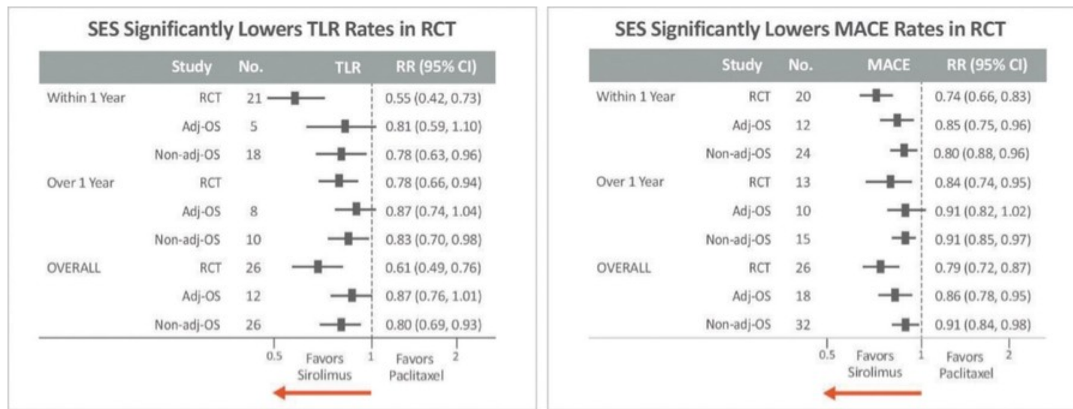
While plain balloon angioplasty can offer significant clinical benefits, it also comes with drawbacks, such as elastic recoil, arterial remodeling or vascular smooth muscle cell excessive proliferation resulting in restenosis (vessel renarrowing) in response to balloon injury. These problems drove the development of bare metal stents ("BMS") that are permanently implanted to hold a vessel open. These devices helped address elastic recoil and remodeling which helped reduce the impact of restenosis while also limiting the incidence of abrupt closure.

While the use of BMS helped address abrupt closure, it did not fully address the problem of restenosis in response to injury caused by the interventional procedure. Both angioplasty and stenting cause a stretch injury to the artery, resulting in a healing response whereby arterial smooth muscle cells proliferate and may block the artery again, a process known as restenosis. Restenosis can also occur over longer periods of time after a procedure because of the development of new atherosclerosis.

To help address the problems of restenosis, device manufacturers introduced drug-eluting stents ("DES"), which are stents coated with potent pharmaceutical agents that stop excessive cellular proliferation and thereby minimize restenosis within the stent (ISR). The most commonly used drugs were sirolimus, 'limus analogs and paclitaxel. Paclitaxel is a cytotoxic drug widely used in cancer chemotherapy. Paclitaxel interferes with cell division, leading to cell death. Sirolimus and other 'limus analogs, on the other hand, are cytostatic drugs widely used as an immunosuppressant to prevent transplant rejection. Sirolimus works by blocking a key pathway critical to cell proliferation while allowing the cell to continue to function when sirolimus is no longer present. Sirolimus and its analogs, or 'limus agents, can be administered in high doses without adverse effects, resulting in a low toxicity profile.

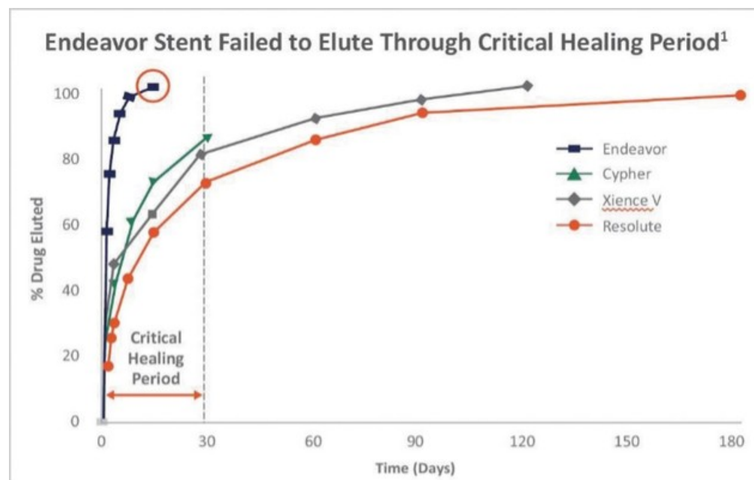
In a large meta-analysis of 76 studies in patients undergoing percutaneous coronary intervention, 'limus-eluting stents outperformed paclitaxel-eluting stents. In a meta-analysis of 26 randomized controlled trials ("RCTs"), 'limus-eluting stents demonstrated superior safety and efficacy with significantly lower MACE and target lesion revascularization, rates compared to

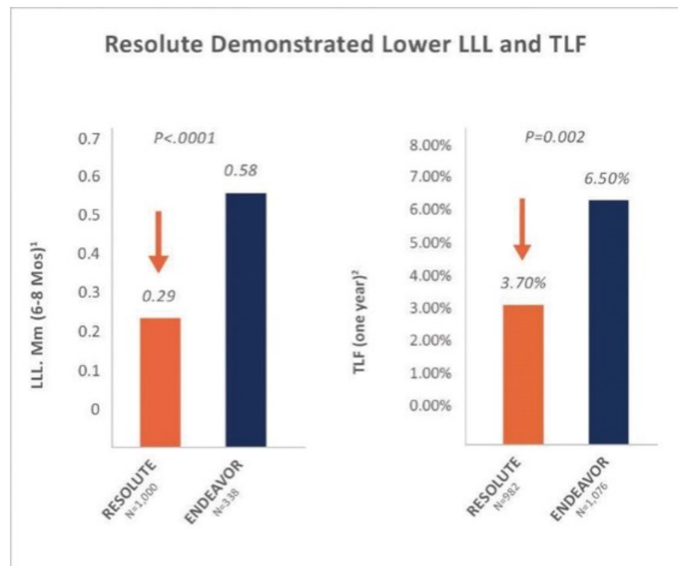
paclitaxel-eluting stents (see figure below). Thus, ‘limus analog eluting stents have become the clear “gold standard,” with nearly 100% current global market share in the coronary DES marketplace.



[1]Xinlin Zhang, et. al. PLOS ONE 2014 May 20;9(5):e97934. Adj-OS = adjusted observational study; CI = confidence interval; No. = number of the studies; Non-adj OS = non-adjusted observational study; PES = paclitaxel-eluting stents; RCT = randomized controlled trial; RR = relative risk; SES = sirolimus-eluting stent; TLR = target lesion revascularization

One demonstrated requirement for the use of sirolimus and other ‘limus agents in DES for the prevention of restenosis is that they be bioavailable for approximately 30 days at the treated lesion for optimal efficacy. This 30-day period is considered the critical healing period following the baseline interventional procedure during which the DES is implanted. For commercially successful DES products marketed by leading companies such as Medtronic, Abbott and Johnson & Johnson, the drug elution profile, or rate at which drug is released from the stent, has been specifically engineered and demonstrated in published preclinical results to provide drug availability for approximately 30 days. The critical importance of this 30-plus day elution profile for sirolimus and ‘limus agents is best demonstrated by Medtronic’s experience with its first DES product called Endeavor. The Endeavor DES was designed to have a faster drug release profile resulting an elution period of approximately 14 days. Clinical results with the Endeavor product were not favorable as compared to other commercially available DES. Subsequently, Medtronic developed and commercialized another DES product called Resolute that eluted Zotarolimus, a ‘limus agent proprietary to Medtronic, over more than 30 days. Medtronic conducted head-to-head clinical studies comparing Endeavor to Resolute demonstrating significantly superior clinical outcomes for Resolute in terms of Late Lumen Loss (“LLL”), and Target Lesion Failure (“TLF”). The figures below show the drug elution profile of the fast-eluting Endeavor DES compared to Resolute and the Cypher DES (Johnson & Johnson) and the Xience DES (Abbott), as well as clinical outcomes comparing Endeavor to Resolute.





[1]Tada, et. Al., Am Heart J. 2013 Jan;165(1):80-6; [2]Leon M. LBCT III, Session 3014. Presented at: ACC 60th Annual Scientific Sessions; April 2-5, 2011

While DES offer significant clinical improvements over plain balloon angiosplasty and BMS, they have limitations, including the need for long-term use of dual antiplatelet therapy (having to use two types of antiplatelet agents) to address the new issues of late and very late stent thrombosis (formation of a blood clot) caused by delayed healing, local inflammation and impaired endothelial function around the stent. In addition, restenosis within a stent occurs in 5-10% of stented patients during the first year and continues at a rate of up to 3% per year thereafter, according to data from the National Cardiovascular Data Registry.

The limitations of DES prompted innovation for improved solutions that enable local delivery of anti-proliferative drugs while not leaving a permanent metal implant in the vessel. Bioabsorbable vascular scaffolds (“**BVS**”), were developed with the objective of performing like stents while eventually dissolving and leaving nothing behind after a few years. In July 2016, the first such device was approved by the FDA, Abbott’s Absorb Everolimus-eluting BVS. Unfortunately, this promising innovation has encountered several setbacks in clinical studies and upon commercialization. In September 2017, Abbott decided to pull Absorb from the market while other device manufacturers halted their in-progress programs. As a result, the attractive concept of “leave nothing behind” drug-eluting interventional therapy for coronary arteries remains unfulfilled. More recently, these devices are being explored for treatment of below-the-knee PAD, a challenging area of unmet need for which we believe Virtue SAB may warrant further development.

Drug-coated balloons have emerged during the last decade with the goal of providing the mechanical vessel expansion and anti-proliferative drug properties of DES while leaving nothing behind. We believe the concept of combining balloon angioplasty with simultaneous delivery of anti-proliferative medication may offer incremental benefits over available interventional therapies by (i) preserving the artery’s original anatomy; (ii) enabling treatment of vessels where DES delivery is challenging, such as small and bifurcated vessels; (iii) offering potential clinical improvement in lesions where available interventional devices have shown poor performance, including below-the-knee and restenotic lesions; and (iv) minimizing the dependency on long-term dual antiplatelet therapy and associated bleeding risks.

While having the potential to offer benefits over available interventional therapies, drug-coated balloons face some important challenges:

- *The Use of Paclitaxel* — Despite the inferior performance observed in DES, most of the drug-coated balloons in use or in development globally deliver paclitaxel. In 2019, a published meta-analysis of several randomized controlled trials raised concerns of increased deaths among patients with femoropopliteal artery disease who received paclitaxel-coated devices (balloons and stents) resulting in the halting of several clinical studies and triggering an FDA investigation. Following careful

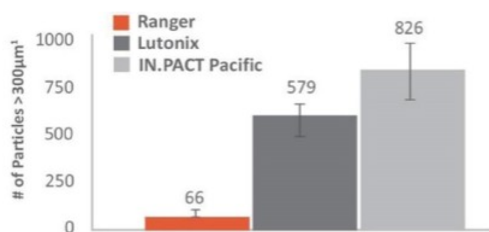
analysis of data gathered from all the manufacturers, in August 2019, the FDA requested manufacturers to update device labeling and clinical study informed consent documents to incorporate information about the late mortality signal and made a commitment to continue working with the manufacturers and investigators on additional clinical evidence development. The primary reason paclitaxel is used on drug-coated balloon technology is that paclitaxel has shown to be an easier pharmaceutical agent for balloon-based delivery due to fast tissue absorption and long tissue retention. On the contrary, ‘limus agents have proven to be quite difficult based on two key reasons: (i) slow tissue absorption making it difficult to transfer the drug and ensure desired tissue absorption; and (ii) short half-life (the time it takes for the amount of drug present to be reduced by 50%) makes it challenging to ensure that therapeutic concentration of the drug is present for the critical, four-week healing period.

Comparison of ‘Limus Agents and Paclitaxel by Key Attributes Relevant to Drug-Coated Balloons

Sirolimus has been Observed to be Superior to Paclitaxel in Clinical Studies but Requires a Novel Approach for Optimal Delivery and Extended Release of Therapeutic Dose Through the Critical Healing Period

Attribute	Sirolimus	Paclitaxel
Mode of Action	Cytostatic ✓	Cytotoxic
Margin of Safety	10,000 Fold ✓	100 Fold
Therapeutic Range	Wide ✓	Narrow
Anti-Restenotic	Yes Lower Late Lumen Loss ✓	Yes
Anti-Inflammatory	Yes ✓	No
Tissue Absorption	**Slow**	✓ **Fast**
Tissue Retention	**Short**	✓ **Long**

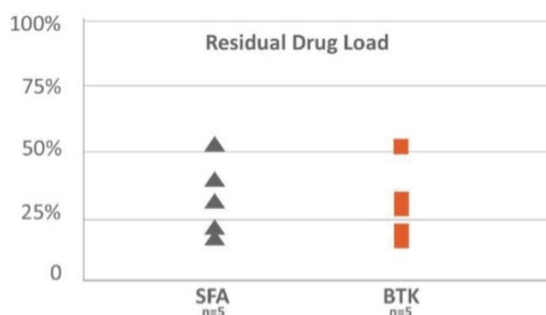
- *The Need for Balloon Surface Coating* — Drug-coated balloons utilize surface coatings for drug delivery which carry inherent limitations such as risk of emboli (*e.g.*, a blood clot or other blockage) from large coating particulates that may cause downstream ischemia (an inadequate blood supply) in non-target tissues. Published quantitative analysis of various drug-coated balloons showed a substantial number of large particles (>300µm). Large particles have the potential to occlude microvessels downstream following balloon inflation.



[1]Agent Paclitaxel-Coated PTCA Balloon Catheter - Boston Scientific - http://www.bostonscientific.com/en-EU/products/balloons--drug-coated/agent/how-trans-pax-works.html. [2]Brodmann: EuroPCR 2015; [3]Sequent Please Neo IFU with similar language in Lutonix IFU

In addition, third-party clinical data demonstrated that 50-80% of drug was washed or scraped off during transit to the target lesion prior to balloon inflation. Concerns of drug loss in transit and risk of particulates have prompted existing drug-coated balloon manufacturers to recommend balloon inflation within 30 seconds of balloon insertion into the patient, making it challenging for

physicians to reach target lesions and ensure proper placement in such a short period of time, particularly in difficult coronary and peripheral lesions such ISR, small vessel disease, and below-the-knee disease.



Targeted Unmet Needs and Market Opportunity for Virtue SAB

We believe significant unmet needs remain in certain artery disease indications where treatment options are limited or fail to adequately improve patient outcomes, including ISR, SV, high bleeding risk patients undergoing percutaneous revascularization and BTK. We estimate these indications currently represent a total addressable global market opportunity of nearly 3.2 million treatable artery disease lesions. Further, based on its estimation of appropriate regional average selling prices, we estimate that the current aggregate annual global market opportunity for Virtue SAB is approximately $3 billion.

The above estimates are based on, among other things, our engagement and work with an established market research firm to conduct market analysis around the VirtueSAB global opportunity. This third party employed both primary and secondary methods for data gathering and analysis. Primary analysis involved multiple Q&A calls with industry-leading key opinion leaders to help assess the addressable patient population and the most addressable patient segments. Secondary data analysis was conducted by mining numerous subscription-based market databases, Medicare data and published literature. After gathering initial disease prevalence data, both we and the third party spent extensive time collaborating on further delineating potential procedure volumes for coronary ISR, coronary SV disease, and BTK peripheral disease that can be addressed by Virtue SAB, taking into consideration patient treatment pathways, anticipated product benefits, competitive landscape and reimbursement. The market size calculations also took into account patients with high bleeding risk, which overlaps with all three target indications and we believe will be an important driver of potential adoption. Third-party data mining, for which references were tracked, combined with our knowledge of market dynamics and anticipated product differentiation, helped us arrive at the global procedure count of 3.2 million. We determined average selling price estimates calculated by country or region based on existing competitive device prices, as well as estimated future pricing for Virtue SAB and future competitive devices. We cross-checked these estimates with Terumo, our strategic partner for Virtue SAB. Using the specific regional market size calculations by indication and the estimated ASPs, we were able to calculate that the future addressable market value for Virtue SAB in its target indications to be at least $3 billion.

- *Coronary ISR:* The vast majority of coronary artery interventional procedures involve the placement of a permanent stent at the site of stenotic lesion. According to data from the National Cardiovascular Data Registry, restenosis within a stent occurs in 5-10% of stented patients during the first year and continues at a rate of up to 3% per year thereafter, resulting in what we currently estimate to be an annual addressable global market of nearly 339,000 lesions that may require treatment. We believe the only device treatments currently approved by the FDA specifically for use in coronary ISR lesions are balloon angioplasty and intravascular radiation therapy known as brachytherapy. However, brachytherapy is considered a last resort treatment due to expense, limited availability, and long-term requirement for dual antiplatelet therapy, and hence represents a small proportion of ISR procedures, while traditional balloon angioplasty has poor outcomes with high retreatment rates. Although DES is not approved for ISR, it is commonly used off-label despite the problems associated with multiple stent layers within the lumen of the vessel along with other limitations.

- *De Novo Coronary Small Vessels (<=2.5 mm)*: DES are difficult to position in vessels measuring less than or equal to 2.5 mm in diameter and may reduce already limited luminal area thereby impacting blood flow. We estimate that there are currently 817,000 lesions in small diameter vessels that may require treatment worldwide.

- *High-bleed Risk in De Novo Lesions (>2.5 mm):* Percutaneous coronary intervention (“PCI”), with placement of DES requires prolonged (greater than six months) treatment with dual antiplatelet therapy (“DAPT”), which is intended to prevent stent thrombosis or the development of blood clots on or around the metal struts of a stent. Stent thrombosis can lead to major adverse events such as heart attacks and death. However, DAPT is associated with an increased risk of major bleeding. For patients undergoing PCI who are identified as being at high risk of bleeding, prolonged DAPT puts them at an increased risk of bleeding. We estimate that patients with an increased risk of bleeding currently have an estimated 817,000 treatable lesions with vessel diameter greater than 2.5 mm.

- *Below-the-Knee Lesions:* BTK disease is a form of PAD and is a primary cause of critical limb ischemia or lack of sufficient blood flow to the legs and feet. This may lead to amputation and increased risk of death. Diagnosis and treatment of BTK disease is highly fragmented with patients being diagnosed by internists, podiatrists as well as interventionalists. The Rutherford score is often used to classify patients with peripheral artery disease with 0 being asymptomatic and 6 being severe ischemic ulcers or gangrene. The patients with Rutherford score of 3-5 are most likely to benefit from an effective interventional BTK treatment. We estimate there are currently 1,242,000 treatable BTK lesions worldwide. Available endovascular treatment options are limited and often provide limited benefit. Balloon angioplasty has generally poor outcomes with high restenosis rates that require frequent retreatment for these lesions. DES and bare metal stents are used off-label to treat BTK lesions but suffer from strut fractures and kinking due to high torsion and potential for a crush injury in arterial lesions that are located between the knee and ankle. Disappointingly, BTK trials with paclitaxel-coated balloons to date have shown limited improvement over plain balloons as well as, in some cases, increased risk of amputation. While the cause of increased amputation risk has not been attributed, we believe this may be due to drug toxicity and the impact of flakes and large particulates from the balloon coating itself causing blockage in downstream capillaries or the cytotoxic effect of paclitaxel in these downstream locations.

Impact Potential of Virtue SAB

Virtue SAB is a proprietary drug/device combination product designed to deliver extended focal release sirolimus during angioplasty for the treatment of atherosclerosis and prevention of restenosis. The patented Virtue SAB is specifically designed to perform angioplasty, a well-established interventional procedure where high-pressure balloon inflation mechanically re-opens a clogged artery. It also simultaneously enables protected delivery and extended focal release of therapeutic levels of proven sirolimus over the critical healing period following angioplasty, revolutionizing intra-procedural arterial drug delivery while leaving nothing permanent behind in the artery. While Virtue SAB is designed to achieve certain results as described above and below, there is no guarantee that Virtue SAB will prove to be safe and effective. Virtue SAB is designed to overcome the limitations of drug-coated balloons by:

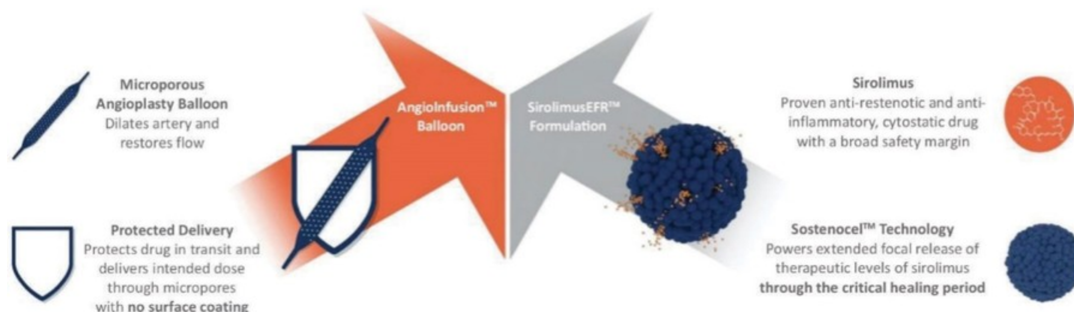
- Delivering sirolimus without the need for a permanent implant or balloon coating;· Protecting drug during transit to treatment site, preventing drug loss and reducing potential for downstream ischemia from large particulates;

- Performing angioplasty using standard catheter techniques without navigation and deployment time constraints; and

- Delivering the intended dose of sirolimus consistently.

Virtue® Sirolimus AngioInfusion™ Balloon (SAB)

Designed to Revolutionize Angioplasty with Protected Drug Delivery while Leaving Nothing Behind



The differentiated design of Virtue SAB was made possible by combining two key technologies:

- Our patented AngioInfusion Balloon is designed to offer protected delivery of SirolimusEFR by keeping the drug formulation contained within the Dose Unit until the time of inflation when it is delivered to the target lesion through micropores in the balloon surface. The AngioInfusion Balloon is designed to offer the following benefits:
  - Enable high-pressure angioplasty to dilate artery, restoring blood flow;
  - Protect SirolimusEFR in transit to deliver the intended therapeutic dose at the target lesion;
  - Deliver SirolimusEFR simultaneously with angioplasty; and
  - Leave no permanent implant behind.
  - Our proprietary, investigational SirolimusEFR powered by Sostenocel, a fully bioabsorbable technology, is designed to enable extended focal release of a therapeutic dose of the anti-restenotic sirolimus over the critical healing period. SirolimusEFR is designed to offer the following benefits:
  - Protection of sirolimus from rapid degradation;
  - Extended release of therapeutic levels of sirolimus into the tissue during the critical healing period of approximately 30 days; and
  - Elimination from the body completely, leaving no residual drug or material behind.

Virtue SAB System Components and Deployment

The Virtue SAB product candidate is under development to be provided in two packages:

- *AngioInfusion Balloon Package:* This package includes the AngioInfusion Balloon along with a Compliance Card explaining the pressures needed for full balloon expansion, a Dose Chart which defines the dose of SirolimusEFR to be utilized for each balloon size, and the proposed Instructions for Use (“IFU”) for the system. To accommodate various vessel sizes and lesion diameters, we expect end users would need to stock an array of AngioInfusion Balloon sizes. The

AngioInfusion Package is expected to be stored at room temperature with target shelf-life of two years at commercial launch (shelf-life independent of SirolimusEFR Package), if approved.

- *SirolimusEFR Package:* This package includes SirolimusEFR in freeze-dried powder form in a vial with all components needed to reconstitute the formulation and set the desired dose to be delivered for the target lesion based on length and vessel diameter according to the Dose Chart and IFU provided in the package. The SirolimusEFR package is designed to be universal for all AngioInfusion Balloon sizes.

Since Virtue SAB is designed to work primarily as a balloon angioplasty catheter, the device most commonly used by interventional cardiologists, we believe it should be relatively easy for physicians to learn, adopt and use the device. The additional steps we expect will be required to reconstitute SirolimusEFR are straightforward and familiar to nurses and technicians. Following the standard preparation of the vessel and after identifying the appropriate balloon size, Virtue SAB is designed to be deployed in three easy steps:

1. *Reconstitute the formulation and set dose*

   - SirolimusEFR is designed to be provided as a lyophilized (freeze-dried) powder that is reconstituted using provided components prior to the angioplasty procedure. Each balloon size is designed to deliver a specific volume of SirolimusEFR. Based on the balloon size selected, the required dose volume of the reconstituted liquid formulation is loaded into the Dose Unit. The SirolimusEFR-loaded Dose Unit is connected to the AngioInfusion Balloon catheter.

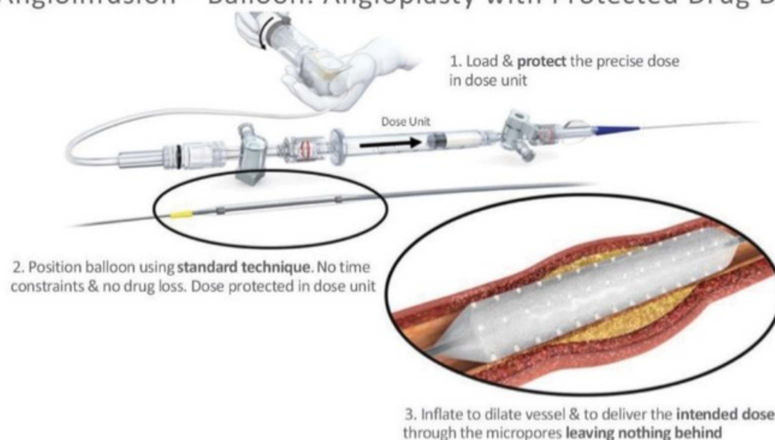
2. *Prime the catheter*

   - The AngioInfusion Balloon is a semi-compliant microporous balloon. After the Dose Unit is connected, the AngioInfusion catheter is primed with the formulation using a standard endoflator device used in all catheterization labs

prior to insertion into the patient and navigation to a target lesion. The dose remains protected in the Catheter and the Dose Unit.

3. *Position AngioInfusion Balloon and Inflate*

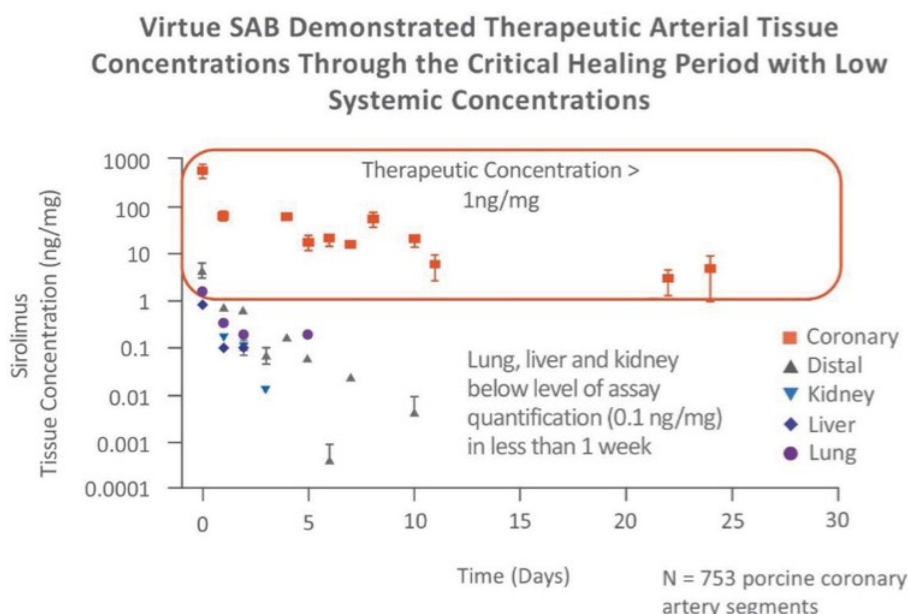
- Similar to standard angioplasty, a guidewire and guide catheter are placed, and the balloon is positioned at the lesion using radiopaque marker bands. When satisfied with device positioning, the physician inflates the AngioInfusion Balloon to perform standard high-pressure angioplasty. The intended dose of SirolimusEFR is delivered simultaneously through the micropores to the target lesion.



Preclinical Data

We have conducted extensive preclinical testing of Virtue SAB and its key enabling technologies (SirolimusEFR and the AngioInfusion Balloon), including feasibility work as well as GLP studies in support of regulatory filings and approvals. This work includes a variety of benchtop as well as small and large animal models. Large animal studies have been conducted in a porcine animal model, a widely used model for testing of interventional cardiovascular devices. A particularly important series of preclinical studies involving 130 pigs and over 750 distinct artery treatment sites showed that Virtue SAB provided extended focal release of therapeutic levels of sirolimus through the critical healing period of approximately four weeks. The data from these preclinical studies was published in the peer-reviewed EuroIntervention Journal in 2016 and showed that Virtue SAB successfully delivered and enabled long-term focal delivery at the treatment site of a therapeutic sirolimus dose (above the 1ng of drug per mg of tissue). This therapeutic dose level has been clinically proven using DES to be safe and efficacious at reducing restenosis during the critical healing period of

approximately 30 days post-procedure. These preclinical studies also showed very low systemic concentrations in cardiac tissue as well as critical organs, such as lung, liver and kidneys, and did not show any adverse local or systemic effects.



Clinical Results

The SABRE, or Sirolimus AngioInfusion (formerly angioplasty) Balloon for Coronary In-Stent REstenosis, first-in-human clinical study was initiated in November 2013 by Caliber Therapeutics, Inc., which is now our subsidiary. SABRE was a prospective, 50-patient feasibility study at nine European centers (Belgium, The Netherlands, Denmark and Latvia), following patients for three years after Virtue SAB treatment, including angiographic follow-up at six months and clinical follow-up at one, two and three years.

Twelve-month follow-up data from the SABRE study, published in *JACC Intervention* in October 2017, demonstrated the clinical study performance of Virtue SAB in what we believe was a very challenging patient population with predominantly long, diffuse restenotic lesions within stents that had been implanted, on average, nearly four years prior to the study enrollment.

Clinicians in the study reported a 100% procedural success rate on a per patient basis (which was defined as the ability to successfully deliver and deploy the device at the lesion site) with Virtue SAB, suggesting the ease of use of the system. The primary safety endpoint was TLF at 30 days. TLF is commonly defined as a combination of MACE, which include cardiac death, target vessel myocardial infarction (“MI”), as well as clinically (symptom) driven target lesion revascularization. The primary performance endpoint was six-month in-segment LLL, measured as the difference in the vessel lumen diameter immediately after the procedure compared to the follow-up at six months.

Revised Per-Protocol Population

A revised per-protocol population was determined based on analysis of procedural data by an independent core lab. This analysis identified 14 cases out the 50 patients treated in the SABRE study that represented serious violations of the established inclusion and exclusion criteria of the protocol for the study. Eight cases were excluded due to excessive proximity to the aorta or major side branches. Three cases were excluded due to treatment of lesions that were longer than available Virtue SAB devices were designed to treat or multiple lesions in the vessel where there was a target lesion. Finally, three cases were excluded due to previously stented restenosis (*i.e.*, the lesion already had two overlapping treatment stents). Overall, these protocol violations and excluded cases

represent a patient population that will not be allowed in the upcoming Virtue ISR-US pivotal clinical study. The remaining 36 patients are referred to herein as the revised per-protocol ("rPP"), population.

Virtue SAB met the primary performance endpoint of the SABRE study with Virtue SAB demonstrating six-month in-segment LLL was 0.12 mm, a positive result as compared to the study target of 0.43 mm. Virtue SAB met the primary safety endpoint with zero reported TLFs at 30 days. The secondary performance endpoint of binary restenosis was also met with Virtue SAB achieving a rate of 2.8%. Revised per-protocol analysis showed a low 2.8% rate of TLF at one-year follow-up and 5.6% at three-year follow up. The increase in TLF after one year was because of the death of one study patient which was reported as multiple organ failure non-cardiac death and adjudicated as non-device and non-procedure related. Over the entire three-year period of the SABRE study, a total of 66 SAEs occurred in 32 of the 50 study patients (64.0%). A total of 29 SAEs in 18 patients were cardiac-related, of which:

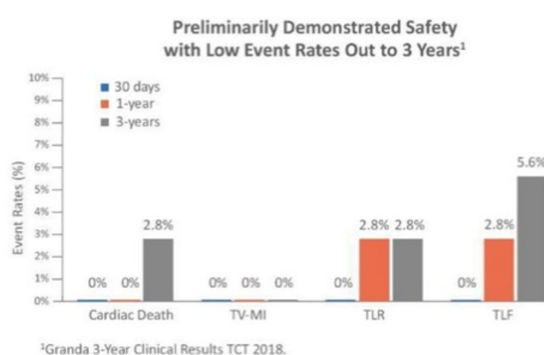
- with respect to their relationship to the investigational device, the SAEs were adjudicated as follows: 19 as "unrelated," three as "unlikely, four as "possible, " two as "probable" and one as "highly probable;" and
- with respect to their relationship to the device treatment procedure, the SAEs were adjudicated as follows: 18 as "unrelated," three as "unlikely," two as "possible," three as "probable" and three as "highly probable."

A total of 37 SAEs in 25 patients were non-cardiac-related, none of them were adjudicated as "highly probable," "probable," or "possible" related to either the device treatment procedure or the investigational device. A total of eleven patients had both, cardiac- and non-cardiac-related SAEs.

Preliminary Efficacy Results Showed Low 0.12mm Late Loss

	Per Protocol[4]
n	36
Reference Vessel Diameter (RVD) mm[1]	2.52 ± 0.32
Minimum Lumen Diameter (MLD) mm	1.96 ± 0.32
% Diameter Stenosis	22.3 ± 9.4
Change in % Diameter Stenosis	5.2 ± 11.4
Late Lumen Loss (LLL) mm[2]	0.12 ± 0.33
Binary Restenosis[3]	2.8%

[1]RVD reported using Internormal values; [2]Trial primary performance endpoint; [3]Trial secondary performance endpoint (binary restenosis = >50% lumen diameter stenosis). [4]Data is based on per protocol population criteria revised to be consistent with proposed Virtue ISR-US pivotal study population.



[1]Granda 3-Year Clinical Results TCT 2018.

Intent to Treat Population

The intent-to-treat ("ITT") population included all the patients enrolled in the study including those treated despite a significant protocol violation as noted above. The ITT analysis of the SABRE study demonstrated 0% MACE and TLF in hospital or at 30 days follow-up, 10.2% MACE and 8.2% TLF at six months, and 16.3% MACE and 14.3% TLF through three-year follow-up. LLL results were 0.31 mm at six months. We believe these results were encouraging given that the ITT population had a high percentage of difficult to treat diffuse lesions as well as lesions with average time since original stent implantation of nearly four years which is substantially longer than typical ISR, which is most likely to occur 3 to 12 months after stenting.

Two-year and three-year clinical follow-up results from the SABRE study were presented at the Transcatheter Cardiovascular Therapeutics ("TCT") conference in 2017 and 2018, respectively. We believe the angiographic and clinical results of the SABRE trial are encouraging and provide the basis for it to conduct the upcoming Virtue ISR-US pivotal clinical study in coronary ISR. The diagrams below summarize the clinical results from this study.

Angiograms of Virtue SAB in Patients

The below images were best matched pairs of baseline and six-month follow-up angiograms identified and are included for illustrative purposes only to show the outcome of Virtue SAB administration in successfully treated patients. The below images are not intended to be representative of all the patients treated in the study and their respective outcomes.

Patient 1 (06-03): Patient presented with an 11.54 mm lesion in the mid-left circumflex artery. Lesion was previously treated with a BMS. The patient's lesion was pre-dilated (a standard practice in drug-eluting balloon procedures) with a non-compliant balloon (a balloon that expands to one specific size independent of internal pressures commonly used to expand clogged arteries) and was treated with a 3.5 mm x 15 mm Virtue SAB. The patient had an excellent post-procedure outcome which was maintained through angiographic follow-up at 193 days. The LLL was measured at -0.03 mm.

Baseline Angiogram | **6 Month Follow-Up**

Patient 2 (11-03): Patient presented with a 17.8 mm diffuse lesion of mid-left arterior descending ("LAD") artery following implantation of a DES seven months prior. After pre-dilatation with a scoring balloon (capable of achieving greater pressures and commonly used to open long, diffuse lesion), the lesion was treated with 3.25mm x 25mm Virtue SAB. The patient had an excellent post-procedure outcome, which was maintained through angiographic follow-up (at 175 days). The LLL was measured at -0.16mm.

Baseline Angiogram | **6 Month Follow-Up**

Global Clinical and Regulatory Program

Per the terms of the Terumo Partnership, we and Terumo plan to execute a global clinical and regulatory program for Virtue SAB for multiple indications, with an initial focus on coronary ISR, coronary SV, and peripheral BTK lesions. Under our agreement with Terumo, it is expected that Terumo will assume financial and execution responsibility for substantially all future clinical and regulatory development with the exception of the Virtue ISR-US trial, the planned U.S. pivotal clinical study to support submission of a PMA application to the FDA for Virtue SAB for treatment of coronary ISR.

In 2019, the FDA confirmed that Virtue SAB will be regulated as a combination product candidate, with the FDA's Center for Devices and Radiological Health as the lead review center of a marketing application. In addition, Virtue SAB has been granted Breakthrough Device designation in:

- *Coronary ISR* — for the balloon dilatation of the stenotic portion (up to 26 mm in length) of a stented coronary artery that is 2.25 mm to 4.0 mm in diameter, for the purpose of improving lumen diameter;
- *Coronary SV* — for the balloon dilation of the de novo stenotic portion (up to 26 mm in lesion length) of a native coronary artery of 2.0 mm to 2.5 mm in diameter (small coronary arteries), for the purpose of improving lumen diameter; and

- *Peripheral BTK* — for the balloon dilatation of the stenotic portion (up to 18 cm in length) of an infrapopliteal artery (P-3 segment or distal, below the knee, with reference vessel diameter 2.25-4.0 mm), for the purpose of improving lumen diameter.

In August, we announced that the FDA granted Orchestra IDE approval with conditions to initiate our planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary ISR. We are permitted to begin enrollment of the study upon completion of standard clinical trial initiation activities including clinical center IRB approvals. The conditional approval also requires us to submit additional information to the FDA.

We currently expect to initiate Virtue ISR-US, the U.S. pivotal clinical study in 2024. This study is expected to randomize 300 patients with coronary ISR lesions previously treated with single layer of stents. Patients are to be randomized in a two-to-one ratio of treatment with Virtue SAB versus plain balloon angioplasty. The primary efficacy and safety endpoint will be TLF at 12-month follow-up. We currently expect to enroll patients at up to 50 study centers in the United States which have already been identified and engaged to participate in the study.

In parallel to the randomized arm of the study, we also plan to enroll a non-randomized study arm of 100 patients with coronary ISR lesions previously treated with a second layer of stents, or double-layer stent coronary ISR. We believe that data from this arm will provide further clinical information in support of potential commercialization of Virtue SAB in the proposed coronary ISR indication. We expect that the primary efficacy and safety endpoint of the double-layer stent coronary ISR arm will also be TLF at 12-month follow-up.

We have already identified and qualified all currently planned study centers for the trial. The Virtue ISR-US study will be further supported by highly qualified third-party resources, including a CRO, an independent core lab and independent imaging analysis lab.

Virtue® SAB Coronary ISR US Pivotal Trial

Randomized Study Arm to Support Regulatory Approval: Single-Layer Coronary In-Stent Restenosis (ISR)

Non-Randomized Study Arm: Double-Layer Coronary ISR

Target Lesion Failure (TLF) defined as target lesion revascularization (TLR), cardiac death (CD), target vessel myocardial infarction (TV-MI)

We currently anticipate using SABRE study results as well as Virtue ISR-US results to support regulatory approval for Virtue SAB for the treatment of coronary ISR outside the United States. In accordance with the Terumo Partnership, we and Terumo have established a Joint Steering Committee (“JSC”) to oversee the development and commercialization of Virtue SAB. We have the right to participate in negotiations with regulatory bodies regarding study designs and other requirements for approval. The Terumo Agreement also provides for ways for us to support further clinical and regulatory development through the active involvement of its team and advisors, and it is anticipated that any such support work provided by us would be reimbursed by Terumo. Through the JSC, our role in regulatory negotiations and other active collaboration with Terumo, we expect to influence, monitor and help drive the execution of the global clinical and regulatory program for Virtue SAB.

SirolimusEFR — Additional Focal Therapies Product Candidates and Development Initiatives

We are also seeking to establish a pipeline of additional targeted therapeutic product candidates for development and future licensing based on our proprietary SirolimusEFR formulation as well as, potentially, the microporous AngioInfusion balloon technology used in the Virtue SAB. SirolimusEFR is an investigational, extended focal release formulation of sirolimus enabled by our proprietary Sostenocel technology. We believe the ability of its Sostenocel technology to enable localized, targeted delivery and extended tissue release of sirolimus offers the potential for new and impactful therapeutic applications of SirolimusEFR. Sirolimus, a pharmaceutical agent also known as rapamycin, is a macrolide compound that is used to treat artery disease (drug-eluting stents or drug-coated balloons), prevent organ transplant rejection, treat rare lung disease called lymphangioleiomyomatosis, and shown to be effective against various tumor types. In addition to these approved indications, sirolimus and its analogs have been studied for potential clinical benefit in a broad array of medical conditions.

Sirolimus and its analogs act to inhibit the mammalian target of rapamycin (“mTOR”), which regulates cellular metabolism, growth, and proliferation. Through its cystostatic mechanism of action, sirolimus prevents cell replication and proliferation while the drug is present in cells and tissues. Unlike cytotoxic agents such as paclitaxel, however, sirolimus does not kill the cells it affects, and these cells return to normal function once the drug is no longer present. This safer anti-proliferative mechanism makes sirolimus a valuable pharmaceutical agent to suppress undesirable immune system activity, which is why systemic use of high doses of sirolimus is the primary treatment to prevent rejection of transplanted organs. It also makes sirolimus useful as an anti-inflammatory and anti-fibrotic agent, which is one of the primary reasons it was chosen as an anti-restenotic drug to coat on the surface of a permanent arterial stent. However, the therapeutics effects of sirolimus are limited by the amount of time sirolimus is present at a therapeutic concentration. The known half-life of sirolimus is short, approximately 62 hours. Sirolimus has an attractive safety profile and a wide therapeutic window which allows for relatively high dosing thresholds before risk of toxicity. However, using systemic delivery of the drug to achieve therapeutic effects in targeted tissues or organs requires regular systemic dosing, increasing the risk of off-target effects and toxicity.

Our proprietary Sostenocel technology is designed to facilitate a localized tissue depot of sirolimus and enable extended focal release of sirolimus over typical critical healing period of approximately 30 days, potentially overcoming the challenges of sirolimus’ short half-life. While our Sostenocel technology is designed to achieve certain results as described above, there is no guarantee that it will prove to be safe and effective.

We retain all rights to develop additional therapies using its proprietary SirolimusEFR to potentially treat focal inflammation outside of coronary and peripheral vascular indications. Further, we are currently working on all CMC testing for its IDE submission for the combination product Virtue SAB that includes populating a drug master file (“DMF”). We intend to follow up post-IDE approval for the Virtue SAB with exploring additional pre-clinical work to support additional clinical indications. Depending on the indication, we may be able to leverage some of the biocompatibility and CMC data in the DMF, while providing additional data depending on the indication selected. Leveraging CMC data in the DMF as well as other preclinical, clinical and device testing work related to Virtue SAB may allow us to advance development of additional SirolimusEFR-based product candidates at an accelerated pace and at reduced cost, although no assurances can be given that development will proceed faster or at lower expense than otherwise expected.

We are evaluating the use of SirolimusEFR through a balloon device treatment and delivery system similar to our AngioInfusion Balloon or simply as a direct focal injection for treatment of additional indications associated with major medical conditions for which mature procedure-based markets already exist. We will seek to identify and initiate discussions with potential strategic partners when we believe sufficient data and evidence is available to support a potential business collaboration.

Therapeutic Medical Device Innovation — Opportunities and Challenges

Opportunities

Therapeutic medical device innovations that can help reduce healthcare costs while improving clinical outcomes are a critical component of successful healthcare delivery and offer future opportunities for clinical and commercial value creation. We were founded on the belief that accelerated development and commercialization of such innovations represents an opportunity to generate significant stockholder value while producing substantial clinical benefit to patients suffering from life-threatening and life-

diminishing medical conditions. The following summarizes several of the key factors we believe are driving the overall therapeutic device market opportunity:

- *Therapeutic medical devices are a core component of the large and growing healthcare industry*. Over the last several decades, therapeutic medical device innovation has dramatically altered the treatment landscape of a broad range of procedure-based medical fields, giving rise to a number of new multi-billion-dollar markets as treatment patterns have shifted to leverage the advantages of new, less invasive and more effective solutions. The U.S. medical device market dominates this global industry, with annual sales reaching $169.1 billion in 2020 according to Analytica. According to a 2022 Fortune Business Insights report, the medical device industry is poised for steady growth, with global annual sales forecasted to rise by over 5 percent annually and reach nearly $720.0 billion by 2029.

- *Growing healthcare expenditures driven by an aging population create a significant need to improve procedural techniques and treatment outcomes while reducing the cost, risk, complexity and recovery time associated with medical procedures for major conditions*. According to the WHO, global healthcare expenditures reached $8.5 trillion in 2019, growing at a rate of 3.9% annually, 30% faster than overall economic growth rates. The extraordinary growth in healthcare spending is driven in part by the ever-increasing demands of a longer-lived, aging population. According to the United Nations, the global population aged 60 years or over numbered 962 million in 2017, more than twice as large as in 1980 when there were 382 million persons aged 60 years or older worldwide. The number of persons aged 60 years or older is expected to double again by 2050, when it is projected to reach nearly 2.1 billion. Further, the number of persons aged 80 years or over is projected to increase more than threefold between 2017 and 2050, rising from 137 million to 425 million worldwide, according to the UN. Advanced therapeutic medical devices can enable minimally invasive, relatively simple procedures to replicate the outcome of highly invasive, complex and expensive surgical procedures that involve higher patient risk and require lengthier recovery periods. Previously difficult-to-treat conditions are easier to treat as innovative therapeutic medical devices become the new standard of care.

- *Rapid advances in enabling technology, the convergence of devices and drugs, and the emergence of bioelectronic and digital medicine as well as robotics offer new and enhanced therapies that drive improved costs and treatment outcomes for patients while addressing unmet clinical needs*. Advances from a broad range of scientific and engineering fields, including miniaturized components, polymers and biomaterials, metallurgy, advanced electronics and optics, robotics, wireless technology, computing and artificial intelligence offer dramatic new capabilities and improvements for therapeutic medical devices. A key enhancement to therapeutic device capabilities has been the ongoing convergence of devices and pharmaceutical drugs to create the rapidly expanding field of combination products that have enabled device makers to enhance therapeutic device performance as well as offer means to target drug delivery to specific focal tissue to improve efficacy and reduce toxicity in patients. More recently, bioelectronic medicine, another emerging field of therapeutic device technology based on applying targeted electrical stimulation and sensing technology to modulate, activate, or regulate neurological or physiological systems, has found expanding applications across multiple large therapeutic device market segments.

Challenges

Despite the substantial and growing need for innovative medical device solutions, significant barriers of cost, time and work prevent many such innovations from reaching patients. Smaller start-up companies that typically develop novel therapies often struggle for resources to reach clinical and commercial value inflection, while large multinational medical device companies have constrained research and development budgets that limit investment in innovation and development-stage acquisitions. Based on data tracking medical device startups during the prior decade, companies that raise capital beyond Series A now require an average of $60 million in funding. In addition, over the last two decades, the medical device industry has undergone significant consolidation, with a similar goal of creating efficiencies as well as to maintain strategic relevance with their customers as hospitals and other providers seek to consolidate and extract savings from their supplier base. This global consolidation of the healthcare ecosystem creates significant challenges for emerging medical device companies, including:

- Large medical device companies and financial investors are prioritizing commercial-stage over preclinical and clinical-stage acquisition and investment opportunities. The large, global medical device consolidators generally pursue capital and resource allocation strategies that place high value on opportunities that can enhance revenue growth without meaningful dilution of near-term profitability. These companies have increasingly focused on acquiring commercial-stage assets over

clinical-stage assets, while reducing their own internal research and development investments in novel, high-risk, high-potential reward innovation programs. The top 20 global medical device companies allocate on average only 7% of revenue to research and development, limiting their ability to spend money both on internal and acquired programs. By contrast, the top 20 biopharmaceutical companies spend an average of 20% of revenue on research and development, giving them much greater ability to invest in new therapeutic innovations as well as to deploy capital into early-stage product candidate development through a range of risk and reward sharing collaborative structures with smaller private and publicly-traded biotechnology companies. According to the SVB Healthcare Report 2019, approximately 85% of venture-backed medical device companies that were acquired by larger companies required commercial traction prior to their acquisition.

- Emerging medical device companies are increasingly required to commercialize their technologies, a process which is both expensive and challenging in a highly consolidated industry, forcing investors to deploy more capital and also prioritize commercial-stage or near commercial-stage companies. The emphasis on later-stage commercial medical device companies by the global medical device consolidators as well as investors creates pressure on medical device innovators to both innovate and commercialize their products. The skill set of the innovator — creativity, efficient problem-solving, engineering, intellectual property development, intelligent risk-taking, understanding clinical and regulatory development pathways — is very different from the skill set required to commercialize medical device innovations. Additionally, products that address high-volume existing procedure-based medical markets are particularly challenging for small companies given that larger, more established competitors are able to deploy much larger direct salesforces and have diverse product portfolios that frequently enable effective product bundling. Overall, organizational transformation for commercialization is challenging, time-consuming, and carries strategic and operational risk. Furthermore, commercialization requires significant additional capital to support supply-chain, inventory, quality management and distribution buildout as well as to fund sales and marketing costs over sustained periods of time before commercial revenues provide sufficient cash-flow contributions. As a result, venture capital investors have similarly chosen to emphasize later-stage investments in medical device companies over early-stage investments. According to Deloitte, Series A funding for medical device companies decreased by 14% from 2006 to 2016 whereas overall venture funding for medical device companies increased by 63% over that same period. Based on data tracking medical device startups during the prior decade, medical device companies require significant capital, with companies that raise capital beyond Series A now requiring an average of at least $60 million in funding.

- Given the cost and resources required to commercialize, most emerging medical device companies focus on a single product and need to achieve revenue scale quickly, which increases overall business risk. Because of the financial and organizational requirements of commercialization and the consequent challenges, innovation-focused companies are typically compelled to limit their focus to a single product or technology platform. As a result, these companies and their stockholders are exposed to concentrated technology, clinical, competitive and market risks. Furthermore, they may need to prioritize capital and resource allocation to commercialization over ongoing product innovation and clinical evidence development, increasing the risk that their core product solution loses competitive advantage or value over time.

Our Growth Strategy

Our growth strategy is primarily focused on the execution of key development initiatives and partnership opportunities within its existing product pipeline, with the objective to advance these product candidates to key value inflection points and to form strategic partnerships for commercial value realization. This includes advancing clinical study activities for our flagship product candidates, as well as moving earlier stage product candidates further into clinical development. In the future, we will look to potentially thoughtfully expand its pipeline through collaborations or spinouts with corporate partners, targeted acquisitions that are made in parallel to forming strategic collaborations, royalty-based research and development partnerships, as well as highly selective organic development or intellectual property licensing. We intend to carefully screen new opportunities utilizing our focused innovation selection criteria to ensure a fit with its partnership-enabled business model.

- ***Target mature therapeutic device markets with significant unmet needs***. Product innovations that address known unmet clinical and procedural needs in established medical markets with entrenched leaders and slowed product innovation.

- ***Provide high-impact, procedure-based solutions with rapid adoption potential***. Transformative technology solutions with the potential to improve clinical outcomes and lower costs of care while fitting existing treatment paradigms and having well-defined development pathways.

- ***Offer strategic and financial benefits to a commercial partner and us***. Innovative technologies that are protected by strong intellectual property offer distinct advantages that can be leveraged to disrupt competitive dynamics, and have the potential to provide attractive profit margins to support favorable partnership economics.

Our Team and Innovation History

We are led by a highly accomplished, multidisciplinary management team with extensive experience and strong expertise in all phases of therapeutic product development. Our senior management team, including the vice president-level and above executives, has over 350 years of combined experience, with an average tenure of 25 years in the development and commercialization of procedure-based innovations for major clinical indications. Our team's expertise includes clinical need and market analysis, product design and intellectual property prosecution, clinical and regulatory execution, as well as supply chain and quality system development. Members of our senior management team have been personally involved in the development and regulatory approval or clearance of over 100 products and have helped author over 600 patent applications. Our executive team is guided by a seasoned and highly accomplished board of directors with knowledge and experience in the healthcare industry, including medical devices, biotechnology and clinical medicine, as well as business operations, strategy, finance and capital markets. Further, our product development efforts are supported by world-renowned medical advisors who are physicians and scientists recognized for their knowledge of specific disease states and treatment options available, as well as their ability to quickly assess new technologies for clinical feasibility and likelihood of adoption.

All of the product candidates in our pipeline were conceived and developed by our management team and employees through predecessor companies founded by a medical device accelerator, Accelerated Technologies, Inc. ("ATI"). ATI was originally founded in 2000 and employed active collaboration with industry-leading physicians to identify and purpose-build transformational therapeutic devices. Our founders and senior executives, Mr. Hochman and Mr. Sherman, joined ATI in 2006 and 2008, respectively. Prior to their joining, ATI was associated with the development of approved devices such as transcatheter aortic valve replacement (Percutaneous Valve Technologies, Inc., which was acquired by Edwards Lifesciences Corp. in 2003) and catheter-based temporary ventricular support (Impella CardioSystems AG, which was acquired by ABIOMED, Inc. in 2005). Mr. Hochman and Mr. Sherman assumed control of ATI in 2009 and proceeded to found new companies that developed Virtue SAB (Caliber Therapeutics), BackBeat CNT (BackBeat Medical), and the FreeHold Duo and Trio Retractors (FreeHold Surgical). Legacy Orchestra's business was formed in May 2018 upon the merger of these three entities and a concurrent recapitalization. ATI was subsequently acquired by Legacy Orchestra in December 2019.

Our Strategic Holdings

We own outright or maintains ownership of minority equity interests, convertible debt and/or royalty-stream interests in additional therapeutic device assets currently undergoing early-stage commercialization and further product development that we believe have growth and value appreciation potential. Our objective is to create and realize additional stockholder value through ownership in innovative therapeutic product solutions in core, adjacent and synergistic medical segments. Our strategic holdings include:

- ***FreeHold Surgical —*** we own 100% of FreeHold Surgical, LLC, which has developed and commercialized on a pilot basis in the U.S. patented single-use FreeHold Hands-Free Intracorporeal Retractions ("FreeHold Devices") designed to help reduce required incisions and enhance laparoscopic and robotic procedures. FreeHold Trio and Duo hands-free intracorporeal retractors are regulated as Class I medical devices by the FDA and are generally indicated for internal organ or tissue retraction during minimally invasive procedures. We believe FreeHold devices are the only fully and continuously adjustable, completely intracorporeal devices specifically designed to address limitations of the available retraction methods. These devices are designed to enable a variety of advanced robotic and laparoscopic surgical procedures for the treatment of obesity, GI disorders and other indications. Versatile design makes retractors appropriate for a broad range of minimally invasive procedures, including bariatric and foregut surgeries, nephrectomies, colectomies, cholecystectomies, paraaortic node dissections, hysterectomies, and other procedures. We believe FreeHold devices are designed to offer several potential advantages over existing retraction options:

- Improve Patient Care

  - No additional incisions required: deployed through same access incisions as used in standard procedures;

  - Minimize complications from suboptimal visualization and additional incisions; and
  - Avoid trauma associated with the use of Nathanson-type retractors
- Enable Full Surgeon Autonomy
  - Surgeon controls positioning and adjustment of retractor;
  - Once positioned, surgeon has full use of both hands to perform surgery; and
  - No coordination with circulator required
- Optimize Visualization
  - Easily adjustable throughout the procedure for sustained visibility; and
  - Low profile design minimizes procedural clutter and collisions

Targeted Commercialization — we estimate over 10,000 procedures using FreeHold devices have been performed in the United States to date, primarily in bariatric (obesity) and foregut (GI, metabolic) surgeries with some initial experience in paraaortic node dissections (gynecologic oncology), nephrectomies (kidney removal) and cholecystectomies (gallbladder removal). FreeHold's targeted commercial development program involves only two dedicated sales representatives targeting hospitals in the United States to demonstrate clinical utility and commercial demand for FreeHold Devices.

Strategic Potential — we believe FreeHold devices have been optimized for strategic partnership because they are highly differentiated, enabling products that fit into current treatment paradigm, are easy to use with a relatively short learning curve and have sufficiently high profit margins that provide potential for partnering to enable a revenue sharing arrangement.

Formation and Conversion to a Limited Liability Company — In May 2018, Legacy Orchestra completed its acquisition of FreeHold Surgical, Inc., a Delaware corporation that has, among other things, the rights to our FreeHold Devices. FreeHold Surgical, Inc. was incorporated in Delaware in May 2010 and began development of its hands-free, intracorporeal retractors for minimally invasive surgery in 2012. In December 2019, Legacy Orchestra converted FreeHold Surgical, Inc., a Delaware corporation, to FreeHold Surgical, LLC, a Delaware limited liability company. References in this prospectus to FreeHold refer to FreeHold Surgical, Inc. prior to its conversion to a limited liability company and to FreeHold Surgical, LLC after its conversion to a limited liability company, as applicable.

- ***Vivasure Medical*** — as of October 6, 2023, we owned a minority equity interest, representing approximately 11.6% in Vivasure Medical Limited, a Galway, Ireland-based company that develops advanced polymer implants and delivery systems, primarily focused on minimally invasive vessel closure in cardiology, interventional radiology and vascular surgery. Vivasure's lead product candidates include is PerQSeal (CE marked) and PerQSeal+, both fully bioabsorbable, patch-based large-bore (12-24 French, 4-8 mm) percutaneous closure devices. In May 2023, Vivasure announced the initiation of enrollment of the PATCH study, a 171 patient pivotal study of PerQSeal+ for large hole closure designed to support FDA approval of the device. Vivasure has recently completed an approximately $20 million Series D financing led by Haemonetics Corporation, U.S. medical device company that also purchased for $10 million, an exclusive option to acquire Vivasure following completion of the PATCH pivotal study. If this potential acquisition proceeds are fully paid, we are expected to receive approximately between $15 and $22 million in cash proceeds (the total amount depending on the achievement of certain milestones). Mr. Hochman, our chief executive officer, serves as a board observer to Vivasure.

- ***Motus GI*** — as of October 6, 2023, we owned a minority interest, representing approximately 10.1% in Motus GI (Nasdaq: MOTS). Motus GI has developed the Pure-Vu® System, a medical device that has been cleared by FDA to help facilitate the cleansing of a poorly prepared gastrointestinal tract during colonoscopy and to help facilitate upper gastrointestinal (GI) endoscopy procedures. The Pure-Vu® System is CE marked in the EU for use in colonoscopy. The Pure-Vu® System integrates with standard and slim colonoscopes, as well as gastroscopes, to improve visualization during colonoscopy and

upper GI procedures while preserving established procedural workflow and techniques. Through irrigation and evacuation of debris, the Pure-Vu® System is designed to provide better-quality exams. Motus GI began commercialization in the fourth quarter of 2019, with the first commercial placements of its second-generation Pure-Vu® System as part of its initial U.S. market launch targeting early adopter hospitals. According to Motus GI's Form 10-Q for the fiscal quarter ended June 30, 2023 (the "Motus Q2 2023 10-Q"), Motus GI (i) has never been profitable and has incurred significant net losses each year since its inception, including a loss of $7.4 million for the six months ended June 30, 2023, (ii) expects to continue to incur net operating losses for the foreseeable future, and (iii) had $8.5 million in cash and cash equivalents and an accumulated deficit of $148.7 million as of June 30, 2023. Motus GI's net cash used in operating activities for the six months ended June 30, 2023 was $7.3 million. In addition, according to the Motus Q2 2023 10-Q, Motus GI has generated minimal revenues, experienced negative operating cash flows and has incurred substantial operating losses that raise substantial doubt about its ability to continue as a going concern.

Motus GI issued a pool of royalty certificates that provided an interest in future Motus GI revenues equal to three percent of net product sales (upon first generating, in the aggregate since its inception, net product sales equal to $20.0 million) and five percent of licensing proceeds (upon first generating, in the aggregate since its inception, licensing proceeds equal to $3.5 million). Royalties with respect to each of net sales and licensing proceeds were capped at a maximum of $30.0 million per year with respect to the entire pool of royalty certificates. We acquired approximately 53% of all the royalty certificates issued by Motus GI, representing an interest in approximately 1.6% of future net sales and 2.7% of future licensing proceeds, in each case subject to the minimum thresholds and caps discussed above. This royalty interest did not expire until the expiration of the last valid patent claim covering Motus GI's products on a country-by-country basis, which expiration with respect to the United States currently is 2037, which date may be extended by the issuance of additional patents. On September 12, 2023, Motus GI and the requisite number of holders of royalty certificates entered into an Amendment Agreement (the "Amendment Agreement"), pursuant to which the royalty certificates were amended to terminate the rights of royalty certificate holders to receive royalties in exchange for an aggregate of 1,323,323 shares of Motus GI common stock. As a result of the Amendment Agreement, we received 701,522 shares of Motus GI common stock in exchange for our royalty certificates.

From December 2016 to April 2023, Mr. Hochman, our chief executive officer, served as Chairman of the board of directors of Motus GI, and as a member of the board of directors until September 2023. Mr. Sherman, our president and chief operating officer, also served on the board of directors of Motus GI from December 2016 to September 2023.

Our Research and Development

We invest in research and development efforts that advance and expand its product pipeline. Our goals are to: (1) deliver on clinical, regulatory and commercial development objectives for Virtue SAB set forth in collaboration with our strategic partner, Terumo; (2) deliver on clinical, regulatory and commercial development objectives for BackBeat CNT set forth in collaboration with our strategic partner, Medtronic; and (3) further develop pipeline product candidates towards future partnerships with potential strategic partners. Our research and development expenses totaled $21.9 million for the year ended December 31, 2022, and $12.9 million and $13.5 million for the years ended December 31, 2021 and December 31, 2020, respectively.

We believe our ability to rapidly develop innovative product candidates is attributable to the dynamic product innovation process that we have implemented, the versatility and leveragability of our core technologies and our partnership-enabled business model that drives our innovation objectives and research and development process. We have recruited and retained engineers and scientists with significant experience in the development of medical devices. We have a pipeline of product candidates in various stages of development that are expected to provide additional strategic opportunities. Our research and development efforts are based at our facilities in New Hope, Pennsylvania and Fort Lauderdale, Florida.

Our Manufacturing and Supply

Bioelectronic Therapies (BackBeat CNT and CNT-HF)

Our wholly owned subsidiary, BackBeat Medical previously contracted with a business unit of Integer under an agreement (the "Integer Agreement"), to develop and manufacture the Moderato device, which consists of an IPG, powered by a primary battery and a programming system integrated by a programmer interface and telemetry wand and a software application capable of programming

standard pacing functions as well as the different parameters of BackBeat CNT. All intellectual property that Integer developed for BackBeat Medical during the performance of the Integer Agreement, whether independently or jointly, and that resulted from or uses BackBeat Medical's technology or intellectual property are owned by BackBeat Medical. Under the Integer Agreement, Integer provided BackBeat Medical a perpetual, royalty-free, fully paid, assignable, world-wide, non-exclusive license for the device-incorporated Integer property, allowing the use of the incorporated Integer property only within BackBeat Medical's field of use (electrical therapies, particularly cardiac pacing for (i) treatment of HTN and (ii) rhythm management in patients that were implanted with a device for the treatment of HTN). We also utilize the services of external consultancy firms for quality and regulatory services related to Moderato devices to supplement its internal capabilities.

Medtronic has completed integration and associated validation and verification testing of AVIM therapy algorithms as a field downloadable addition to its premium, commercially available dual-chamber pacemaker systems for use in the pivotal study. Medtronic is also providing clinical and regulatory resources in support of the pivotal study. We are reimbursing Medtronic at cost for these development, clinical and regulatory resources. Medtronic will integrate AVIM therapy, at our cost, as a firmware component of a premium pacemaker for regulatory approval and commercialization of AVIM therapy-enabled commercial devices.

Focal Therapies (Virtue SAB, SirolimusEFR and Sostenocel)

Microporous AngioInfusion Balloon and other device components of Virtue SAB. Under the terms of our agreement with Terumo, Terumo has agreed to assume responsibility for managing the supply chain associated with the Microporous AngioInfusion Balloon and other device components used in Virtue SAB prior to commercialization. Currently, these devices are manufactured by a selected group of third parties contracted by us. We are currently in the process of transitioning management of the device supply chain and its various vendors to Terumo. We expect this process to continue through the completion of the Virtue ISR-US trial. All of Virtue SAB's key suppliers and vendors carry the proper quality system certification and/or FDA approvals for the activity they are providing in support of the manufacturing, testing, storage and distribution of components, materials, services or final product.

SirolimusEFR. We have internal capabilities for small scale production (300 vials per run), lyophilization, and characterization testing for SirolimusEFR. Clinical and commercial production has been contracted through an established clinical manufacturing organization with large scale cGMP production capabilities. We have scaled clinical production with an external manufacturing partner to achieve a capacity of approximately 3,000 vials per run with further scaling planned to reach planned commercial production capacity. Additional contract vendors provide polymer synthesis capabilities based on world-class polymer expertise in order to supply enabling components to the Sostenocel technology used to create SirolimusEFR. cGMP syntheses have been performed, with extensive analytical method and quality control development complete. Synthesis of custom polymers has successfully achieved clinical scale with ongoing work to scale processes to commercial scale.

FreeHold Devices

We utilize an FDA-registered and ISO 13485-certified U.S.-based manufacturing partner to manufacture FreeHold Duo and Trio intracorporeal retractors. Our manufacturing partner also provides warehousing and distribution of its products to qualified customers based on orders placed by customers to its FreeHold Surgical subsidiary. We have utilized the same manufacturing partner since the time of FDA product registration. Further, our manufacturing partner has achieved a greater than 99% on-time order delivery rate to our customers.

Our Competition

The medical device industry is intensely competitive, subject to rapid change and significantly affected by new product introductions and other market activities of industry participants. We compete or plan to compete with developers, manufacturers and distributors of cardiovascular and other medical devices. With regard to Virtue SAB, our most notable competitors in the highly competitive interventional cardiology field include Medtronic plc, Becton Dickinson, Boston Scientific Corporation, Philips N.V., B. Braun, Abbott Laboratories, BIOTRONIK, Inc., Concept Medical, Inc., MedAlliance S.A., Surmodics, Inc., Cardiovascular Systems, Inc., MicroPort, Mercator MedSystems, Inc. and others. With regard to BackBeat CNT, our most notable competitors in the highly competitive field of device therapies for HTN as well as cardiac rhythm management devices include Abbott Laboratories, Boston Scientific Corporation, BIOTRONIK, Inc., MicroPort CRM, ReCor Medical, cvRx, Inc., Vascular Dynamics, Inc., Ablative Solutions, Inc. and others. Many of these competitors are large, well-capitalized companies with significantly greater market share and resources than we have. As a consequence, they are able to spend more on product development, marketing, sales and other product

initiatives than we can. We also compete with smaller medical device companies that have single products or a limited range of products. Some of these competitors have:

- significantly greater name recognition;
- broader or deeper relations with healthcare professionals, customers and third-party payors;
- more established distribution networks;
- additional lines of products and the ability to offer rebates or bundle products to offer greater discounts or other incentives to gain a competitive advantage;
- greater experience in conducting research and development, manufacturing, clinical studies, marketing and obtaining regulatory clearance, certification or approval for products; and
- greater financial and human resources for product development, sales and marketing and patent prosecution.

We believe that our proprietary Virtue SAB, BackBeat CNT and other pipeline technologies, our partnership-enabled business model, our strategic partnerships, such as the Terumo Partnership for Virtue SAB and the Medtronic Collaboration for BackBeat CNT, and our organizational culture and strategy, will be important factors in our future success. We compete primarily on the basis that our products are designed to improve outcomes, reduce complications and provide distinct commercial advantages that can be leveraged by us and our strategic partners. Our continued success depends on our, and in some cases, our strategic partners' ability to:

- develop innovative, proprietary products that can cost-effectively address significant clinical needs in a manner that is safe and effective for patients and easy to use for physicians;
- continue to innovate and develop scientifically advanced technology;
- forge risk and reward sharing partnerships with established commercial market leaders to help support product development and commercialization;
- obtain and maintain regulatory clearances, certifications or approvals;
- demonstrate efficacy in sponsored and third-party clinical studies;
- obtain and maintain adequate reimbursement for procedures using its products;
- apply technology to develop pipeline product candidates for additional clinical indications;
- attract and retain skilled research and development and sales personnel; and
- cost-effectively manufacture and successfully market and sell products.

Our Intellectual Property

Our success depends in part on our ability to obtain, maintain, protect and enforce our proprietary technology and intellectual property rights, and, in particular, our patent rights, as well as our ability to preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and other intellectual property rights of third parties. We rely on a combination of patent, trademark, trade secret, copyright and other intellectual property rights and take measures to protect the intellectual property rights that we consider important to our business.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent

application in the applicable country. In the United States, a patent's term can be extended to recapture a portion of the USPTO's delay in processing the patent to issue as well as restore a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. We cannot be sure that our pending patent applications that we have filed or may file in the future will result in issued patents, and we can give no assurance that any patents that have issued or might issue in the future will protect our current or future products, will provide us with any competitive advantage, and will not be challenged, invalidated, or circumvented.

We also rely on trade secret know-how and continuing technological innovation to develop and maintain its competitive position. We seek to protect our proprietary rights through a variety of methods, including confidentiality agreements and proprietary information agreements with suppliers, employees, consultants and others who may have access to its proprietary information. However, trade secrets and proprietary information can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets and proprietary information, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our competitors may independently discover or develop the same trade secrets and proprietary information as us. To the extent that our suppliers, employees, consultants and others use intellectual property owned by others in their work for us, we may be subject to allegations of infringement and further disputes may arise as to the rights in related or resulting improvements, know-how and inventions.

Our success also depends in part on not infringing the intellectual property rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to intellectual property rights that we may require to develop or commercialize our future product candidates may have an adverse impact on the business. If third parties have prepared and filed patent applications in the United States prior to March 16, 2013 (the date when U.S. patent law changed from granting rights to the first-to-invent to the first-to-file) that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. For more information regarding the risks related to our intellectual property, please see the section titled "*Risk Factors — Risks Related to Our Intellectual Property.*"

Below is a more specific overview of our intellectual property as it relates to our pipeline programs by modality:

Bioelectronic Therapies (BackBeat CNT and CNT-HF)

BackBeat CNT and CNT-HF are protected by an intellectual property portfolio which currently includes 39 issued U.S. patents and 68 issued patents in countries outside of the United States encompassing devices, algorithms, and methods. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2025 and 2038, without taking potential patent term extensions or adjustments into account. Additional patent applications are filed on a regular basis. BackBeat issued patents are divided between CNT and CNT-HF as follows: 36 issued U.S. patents and 58 issued patents in countries outside of the United States protect CNT, and which are exclusively licensed to Medtronic in the Primary Field pursuant to the Medtronic Agreement; three issued U.S. patents and 10 issued patents in countries outside of the United States protect CNT-HF; and a further 25 patent applications were filed protecting BackBeat CNT (22 patent applications) and CNT-HF (three patent applications).

In addition to customary early termination provisions, the Medtronic Agreement will terminate on the date no further revenue share payments are due under the Medtronic Agreement and Medtronic's license under the Medtronic Agreement would become fully paid up, perpetual, irrevocable and royalty-free. Revenue share payments with respect to each applicable country (or group of countries) are to be paid for a minimum period of time determined by the latest to occur of (a) the expiration of the last valid claim of certain specified patents (as well as any patents claiming priority to, from or through such patents) (the "Patent-Based Expiration") or

(b) the date that is 12 years after the first commercial sale of any Backbeat CNT-enabled pacemakers in the applicable country or group of countries (the “Time-Based Revenue Share Expiration”). While revenue share payments under the Medtronic Agreement could extend beyond the Time-Based Share Expiration, it is not expected that the first commercial sale of a Backbeat CNT-enabled pacemaker will occur before 2026. Accordingly, to the extent BackBeat CNT-enabled pacemakers receive regulatory approval and are sold commercially, Medtronic’s obligation to make payments to us will extend to at least approximately 2038 under the Time-Based Share Expiration, regardless of the expiration any of our patents. Further, such date may be extended up to an additional five years based on the Medtronic Agreement which provides that the Patent-Based Expiration may be extended until the expiration of patents that may be issued based on additional patent applications that we have filed prior to entering into the Medtronic Agreement, although no assurance can be given that such patents will be issued or any claims associated with newly issued patents will be valid. To the extent there are revenue share payments made under the Medtronic Agreement after the Time-Based Revenue Share Expiration and prior to the Patent-Based Expiration, those payments would likely be based on intellectual property we develop in the future, and not the current patents held by us.

BackBeat CNT and CNT-HF are also protected by trade secrets and proprietary know-how. We seek to protect its proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with its employees, consultants, scientific advisors, contractors and commercial partners.

We will continue to endeavor to obtain and maintain patent protection worldwide on select patentable aspects of BackBeat CNT and CNT-HF as well as to protect our trade secrets and proprietary know-how.

Focal Therapeutics (Virtue SAB, SirolimusEFR and Sostenocel)

We rely on intellectual property protection for Virtue SAB and its enabling technologies, including SirolimusEFR and the AngioInfusion Balloon, based on protection of proprietary particle drug encapsulation technology through trade secrets and proprietary know-how; and through issued patents and patent applications in process covering key aspects of Virtue SAB’s micro-porous balloon system and integration of its drug encapsulation formulation with the device.

Virtue SAB is currently protected by six issued U.S. patents and 20 issued patents outside the United States with additional patent applications pending in the United States and in countries outside of the United States covering key aspects of Virtue SAB product design, clinical application and enabling technology. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2028 and 2032, without taking potential patent term extensions or adjustments into account. The foregoing patents are exclusively licensed to Terumo for the Subject Indications during the term of the Terumo Agreement. We will continue to selectively advance certain aspects of Virtue SAB toward submission of appropriate patent applications. A further nine published patent applications were filed to protect Virtue SAB.

Pursuant to the Terumo Agreement, we share in all of Terumo’s Virtue SAB revenues during the term of the agreement through future royalties of 10-15% of net sales of Virtue SAB, and additional per unit payments for SirolimusEFR used in Virtue SAB for which we are the sole exclusive supplier. The initial term of the Terumo Agreement expires on the tenth anniversary of the date on which the first PMA is obtained from the FDA for Virtue SAB for ISR, and thereafter automatically extends for five-year periods unless terminated by Terumo. Payments under the Terumo Agreement are not tied to the expiration of our patents.

Our Sostenocel technology and SirolimusEFR are intentionally protected by trade secrets and proprietary know-how, as we believe the design and manufacture of this formulation would be highly difficult to develop or reverse engineer. Seeking patent protection for these processes would have required detailed publication of proprietary information without certainty of patent claim issuance or protection.

Development and production of SirolimusEFR have been refined and scaled to support the Virtue ISR-US trial and other trials we plan to conduct to support commercialization of SirolimusEFR. Production scaling and manufacturing processes are central components of the proprietary trade secret and proprietary know-how of the intellectual property protection of Virtue SAB and other future product candidates involving SirolimusEFR.

Virtue SAB is also protected by trade secrets and proprietary know-how that was intentionally not made public or published in patent applications. We believe the strategy to avoid publication of proprietary methods as long as possible has been an important part of maintaining the differentiation and advantages of Virtue SAB. Trade secrets and proprietary know-how include aspects of

formulation, materials production, and manufacturing of Virtue SAB. Such trade secrets and proprietary information is used to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with its employees, consultants, scientific advisors, contractors and commercial partners.

We will continue to endeavor to obtain and maintain patent protection worldwide on select patentable aspects of Virtue SAB as well as to protect our trade secrets and proprietary know-how.

FreeHold Devices

Our FreeHold Devices and additional minimally invasive surgery enabling devices are protected by an intellectual property portfolio which currently includes issued U.S. patents and pending U.S. applications and issued patents and pending applications in countries outside of the United States covering methods and apparatus for intracorporeal retraction and removal of organs, internal adjustment of device and retraction, as well as design for safe device removal. Specifically, this portfolio includes 14 issued U.S. patents, 24 issued patents in countries outside the United States, and several pending applications. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2030 and 2037, without taking potential patent term extensions or adjustments into account. A further seven published patent applications were filed to protect FreeHold devices.

Material Patents

As of October 6, 2023, we owned 171 patents globally, of which 59 were issued U.S. patents and 112 were patents outside of the United States.

Our issued patents expire between February 2025 and May 2037. Despite the near-term expiration of certain of our material patents, we believe that our other patents, as well as our trade secrets and continuing technological know-how, provide us with sufficient intellectual property protection to develop our product candidates and protect our intellectual property.

Our material patents, as of October 6, 2023, their jurisdiction, expiration date and the product to which they relate, are listed in the tables below:

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	9,008,769	8/31/2033	BackBeat CNT
United States	9,333,352	3/14/2033	BackBeat CNT
United States	9,526,900	8/31/2033	BackBeat CNT
United States	9,370,662	8/31/2033	BackBeat CNT
United States	9,656,086	3/14/2033	BackBeat CNT
United States	9,878,162	8/31/2033	BackBeat CNT
United States	9,937,351	7/4/2034	BackBeat CNT
United States	10,071,250	3/14/2033	BackBeat CNT
United States	10,252,061	8/31/2033	BackBeat CNT
United States	10,441,794	3/14/2033	BackBeat CNT
United States	10,485,658	5/16/2037	BackBeat CNT
United States	10,610,689	3/14/2033	BackBeat CNT
United States	10,967,188	7/21/2034	BackBeat CNT
United States	11,097,108	12/19/2033	BackBeat CNT
United States	11,426,589	3/17/2038	BackBeat CNT
United States	11,452,875	3/14/2033	BackBeat CNT
United States	11,712,567	8/31/2033	BackBeat CNT
Europe	EP2934669	12/19/2033	BackBeat CNT
Great Britain	EP2934669	12/19/2033	BackBeat CNT
France	EP2934669	12/19/2033	BackBeat CNT
Germany	EP2934669	12/19/2033	BackBeat CNT
Switzerland	EP2934669	12/19/2033	BackBeat CNT
Sweden	EP2934669	12/19/2033	BackBeat CNT
Italy	EP2934669	12/19/2033	BackBeat CNT
Spain	EP2934669	12/19/2033	BackBeat CNT
Europe	EP3082949	6/17/2034	BackBeat CNT
Great Britain	EP3082949	6/17/2034	BackBeat CNT
France	EP3082949	6/17/2034	BackBeat CNT
Germany	EP3082949	6/17/2034	BackBeat CNT
Switzerland	EP3082949	6/17/2034	BackBeat CNT
Sweden	EP3082949	6/17/2034	BackBeat CNT
Europe	EP3238777	12/19/2033	BackBeat CNT
Great Britain	EP3238777	12/19/2033	BackBeat CNT
France	EP3238777	12/19/2033	BackBeat CNT
Germany	EP3238777	12/19/2033	BackBeat CNT
Switzerland	EP3238777	12/19/2033	BackBeat CNT
Sweden	EP3238777	12/19/2033	BackBeat CNT
Europe	EP3461531	6/17/2034	BackBeat CNT
Great Britain	EP3461531	6/17/2034	BackBeat CNT
France	EP3461531	6/17/2034	BackBeat CNT
Germany	EP3461531	6/17/2034	BackBeat CNT
Switzerland	EP3461531	6/17/2034	BackBeat CNT
Sweden	EP3461531	6/17/2034	BackBeat CNT
Europe	EP3639888	12/19/2033	BackBeat CNT
Great Britain	EP3639888	12/19/2033	BackBeat CNT
France	EP3639888	12/19/2033	BackBeat CNT

Jurisdiction	Patent No.	Expiration Date	Related Product
Germany	EP3639888	12/19/2033	BackBeat CNT
Switzerland	EP3639888	12/19/2033	BackBeat CNT
Sweden	EP3639888	12/19/2033	BackBeat CNT
Europe	EP3445443	4/21/2037	BackBeat CNT
Great Britain	EP3445443	4/21/2037	BackBeat CNT
France	EP3445443	4/21/2037	BackBeat CNT
Germany	EP3445443	4/21/2037	BackBeat CNT
Switzerland	EP3445443	4/21/2037	BackBeat CNT
Sweden	EP3445443	4/21/2037	BackBeat CNT
China	ZL201380072479.3	12/18/2033	BackBeat CNT
China	ZL201480075987.1	6/16/2034	BackBeat CNT
China	ZL2017109301826	12/18/2033	BackBeat CNT
China	ZL2018113777986	6/16/2034	BackBeat CNT
Hong Kong	HK1226016	6/16/2034	BackBeat CNT
Hong Kong	HK1243968	12/18/2033	BackBeat CNT
Australia	AU2013361318	12/19/2033	BackBeat CNT
Australia	AU2014367229	6/17/2034	BackBeat CNT
Australia	AU2018217270	12/18/2033	BackBeat CNT
Australia	AU2019204758	6/17/2034	BackBeat CNT
Australia	AU2017252310	4/21/2037	BackBeat CNT
Canada	CA2893222	12/19/2033	BackBeat CNT
Canada	CA2933278	6/17/2034	BackBeat CNT
Japan	JP6457530	6/17/2034	BackBeat CNT
Japan	JP6510421	12/19/2033	BackBeat CNT
Japan	JP6381087	12/19/2033	BackBeat CNT
Japan	JP6839163	6/17/2034	BackBeat CNT
Japan	JP7050693	4/21/2037	BackBeat CNT
Japan	JP7138202	12/19/2033	BackBeat CNT
Korea	KR10-2221586	12/19/2033	BackBeat CNT
Korea	KR10-2323562	6/17/2034	BackBeat CNT
Korea	KR10-2367191	12/19/2033	BackBeat CNT
Korea	KR10-2471841	6/17/2034	BackBeat CNT
India	401318	12/19/2033	BackBeat CNT
India	409845	4/21/2037	BackBeat CNT
United States	7,869,874	11/7/2028	BackBeat CNT
United States	8,515,536	3/15/2028	BackBeat CNT
United States	8,340,763	3/25/2031	BackBeat CNT
United States	8,165,674	7/13/2029	BackBeat CNT
United States	8,521,280	3/1/2026	BackBeat CNT
United States	9,370,661	9/25/2030	BackBeat CNT
United States	9,427,586	11/15/2027	BackBeat CNT
United States	9,687,636	3/1/2026	BackBeat CNT
United States	9,731,136	9/8/2029	BackBeat CNT
United States	10,252,060	9/8/2029	BackBeat CNT
United States	10,369,333	9/27/2026	BackBeat CNT
United States	11,083,894	9/8/2029	BackBeat CNT
United States	11,529,520	11/15/2027	BackBeat CNT
United States	11,577,059	9/27/2026	BackBeat CNT
United States	11,759,639	10/30/2029	BackBeat CNT
United States	8,086,315	7/3/2026	BackBeat CNT
United States	8,428,729	2/11/2025	BackBeat CNT
United States	9,320,903	10/19/2025	BackBeat CNT
United States	10,232,183	3/22/2025	BackBeat CNT
United States	11,406,829	10/4/2026	BackBeat CNT
United States	10,342,982	9/8/2036	CNT-HF

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	10,596,380	11/15/2027	CNT-HF
United States	11,389,658	9/8/2036	CNT-HF
Australia	AU2016319787	9/9/2036	CNT-HF
Japan	JP6999545	9/9/2036	CNT-HF
China	ZL2016800526048	9/9/2036	CNT-HF
Europe	EP3347090	9/9/2036	CNT-HF
Great Britain	EP3347090	9/9/2036	CNT-HF
France	EP3347090	9/9/2036	CNT-HF
Germany	EP3347090	9/9/2036	CNT-HF
Switzerland	EP3347090	9/9/2036	CNT-HF
Sweden	EP3347090	9/9/2036	CNT-HF
Italy	EP3347090	9/9/2036	CNT-HF
Spain	EP3347090	9/9/2036	CNT-HF

Material Caliber Patents

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	8,696,644	3/9/2032	Virtue SAB
United States	8,715,230	12/30/2030	Virtue SAB
United States	9,649,478	12/30/2030	Virtue SAB
United States	9,649,479	12/30/2030	Virtue SAB
United States	10,207,084	1/6/2031	Virtue SAB
United States	10,806,909	1/6/2031	Virtue SAB
Australia	AU2010339379	12/30/2030	Virtue SAB
Australia	AU2014202452	12/30/2030	Virtue SAB
Australia	AU2016202636	12/30/2030	Virtue SAB
Australia	AU2017225072	12/30/2030	Virtue SAB
Australia	AU2019202994	12/30/2030	Virtue SAB
Australia	AU2020281081	12/30/2030	Virtue SAB
China	ZL201080064442.2	12/30/2030	Virtue SAB
China	ZL201822023030.0	12/4/2028	Virtue SAB
Japan	JP5553908	12/30/2030	Virtue SAB
Canada	CA02786282	12/30/2030	Virtue SAB
Canada	CA3065396	12/30/2030	Virtue SAB
India	IN385350	12/30/2030	Virtue SAB
Europe	EP2603274	12/30/2030	Virtue SAB
Great Britain	EP2603274	12/30/2030	Virtue SAB
France	EP2603274	12/30/2030	Virtue SAB
Germany	EP2603274	12/30/2030	Virtue SAB
Switzerland	EP2603274	12/30/2030	Virtue SAB
Sweden	EP2603274	12/30/2030	Virtue SAB
Italy	EP2603274	12/30/2030	Virtue SAB
Spain	EP2603274	12/30/2030	Virtue SAB
Netherlands	EP2603274	12/30/2030	Virtue SAB

Trademarks

As of October 6, 2023, we have 7 trademarks that are approved in the United States and are in different phases of approvals outside the USA: “Orchestra BioMed,” “OBIO”, “Moderato,” “Virtue”, “FreeHold Surgical,” “FreeHold Duo,” and “FreeHold Trio.” A further 9 applications for trademark registration are pending, covering “SirolimusEFR”, “AngioInfusion”, “Virtue Sirolimus AngioInfusion Balloon,” “BackBeat Medical”, “BackBeat CNT,” “BackBeat Cardiac Neuromodulation Therapy,” “Sostenocel,” “FreeHold Duo,” and “FreeHold Trio.” This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos,

artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our right or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Government Regulation

Our BackBeat CNT and CNT-HF product candidates and our FreeHold Devices, as well as the PerQSeal and Pure-Vu products, are regulated as medical devices. Our Virtue SAB product candidate is a proprietary drug/device combination product candidate in development for the treatment of artery disease. In the United States, products composed of components that would normally be regulated under different types of regulatory authorities, and frequently by different centers at the FDA, are known as combination products. In the case of Virtue SAB, if marketed individually, the balloon angioplasty device would be regulated by FDA as a medical device while SirolimusEFR would be regulated by the FDA as a drug. However, under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The designation of a lead center generally obviates the need for separate approval of each component of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug/device combination product is attributable to the device product, the FDA center responsible for pre-market review of the device product would have primary jurisdiction for the combination product. A combination product with a medical-device primary mode of action generally would be reviewed and approved pursuant to the medical device approval processes set forth under the FDCA. In reviewing the marketing application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the drug component of the combination product met applicable requirements regarding safety and effectiveness. In addition, under FDA regulations, drug/device combination products are subject to cGMP requirements applicable to both drugs and devices, including the QSR applicable to medical devices.

In 2019, the FDA confirmed that Virtue SAB will be regulated as a combination product candidate, with the FDA's Center for Devices and Radiological Health as the lead review center of a marketing application. We expect to seek FDA approval of Virtue SAB through submission of a PMA, reviewed by the FDA's Center for Devices and Radiological Health, for each proposed indication, and does not expect that the FDA will require a separate marketing authorization for each constituent component of Virtue SAB. We anticipate that our standalone SirolimusEFR product candidate for certain potential indications such as ophthalmic inflammatory conditions (uveitis) and chronic joint inflammation (osteoarthritis) will be regulated by the FDA as a drug.

Medical Device Regulation

United States

Medical devices are subject to extensive and ongoing regulation by the FDA under the FDCA and its implementing regulations, as well as other federal and state regulatory bodies in the United States and comparable authorities in other countries under other statutes and regulations. The laws and regulations govern, among other things, product design and development, preclinical and clinical testing, manufacturing, packaging, labeling, storage, recordkeeping and reporting, clearance or approval, marketing, distribution, promotion, import and export and post-marketing surveillance. Failure to comply with applicable requirements may subject a device and/or its manufacturer to a variety of administrative sanctions, such as issuance of warning letters, import detentions, civil monetary penalties and/or judicial sanctions, such as product seizures, injunctions and criminal prosecution.

FDA's Approval Requirements

Unless an exemption applies, each medical device commercially distributed in the United States will require either FDA clearance of a 510(k) pre-market notification, or approval of a PMA application. BackBeat CNT and CNT-HF product candidates will be regulated as Class III medical devices and will require submission of a PMA supplement or a PMA. We also anticipate that our Virtue SAB product candidate will be regulated as a drug/device combination product that will require submission of a PMA.

PMA Pathway

In the United States, medical devices are classified into one of three classes — Class I, Class II or Class III — depending on the degree of risk associated with each medical device and the extent of manufacturing and regulatory control needed to provide

reasonable assurance of safety and effectiveness. Class I devices are deemed to be low risk and are those for which safety and effectiveness can be assured by adherence to the FDA's General Controls for medical devices, which include compliance with the applicable portions of the QSR, facility registration and product listing, reporting of adverse medical events and truthful and non-misleading advertising and promotion. Most Class I devices are classified as exempt from pre-market notification requirements and therefore may be commercially distributed without obtaining prior authorization from the FDA. Class II devices are subject to the FDA's General Controls and special controls intended to provide reasonable assurance of safety and effectiveness of the device. Special controls can include performance standards, post-market surveillance, patient registries and guidance documents. Manufacturers of most Class II devices are required to submit to the FDA a pre-market notification under Section 510(k) of the FDCA requesting permission to commercially distribute the device. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, devices that utilize new technology, or devices deemed not substantially equivalent to a previously cleared 510(k) device, are placed in Class III, generally requiring approval of a PMA application.

Class III devices such as the BackBeat CNT and CNT-HF product candidates require PMA approval before they can be marketed, although some pre-amendment Class III devices for which FDA has not yet required a PMA are cleared through the 510(k) process. The PMA application process is much more demanding than the 510(k) clearance process. A PMA application must be supported by extensive data, including but not limited to technical, preclinical, clinical studies, manufacturing and labeling, to demonstrate to the FDA's satisfaction reasonable evidence of safety and effectiveness of the device. The PMA application must also contain a full description of the device and its components, a full description of the methods, facilities and controls used for manufacturing and proposed labeling.

After a PMA application is submitted, the FDA has 45 days to determine whether the application is sufficiently complete to permit a substantive review and thus whether the FDA will file the application for review. The FDA has 180 days under the FDCA to review a filed PMA application, although the review of an application generally occurs over a significantly longer period of time and can take up to several years. During this review period, the FDA may request additional information or clarification of the information already provided.

Also, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. Although the FDA is not bound by the advisory panel's decision, the panel's recommendations are important to the FDA's overall decision-making process. In addition, the FDA may conduct a preapproval inspection of the manufacturing facility to ensure compliance with the QSR. The agency also may inspect one or more clinical sites to assure compliance with FDA's regulations.

Upon completion of the PMA review, the FDA may: (i) approve the PMA which authorizes commercial marketing with specific prescribing information for one or more indications, which can be more limited than those originally sought; (ii) issue an approvable letter which indicates the FDA's belief that the PMA is approvable and states what additional information the FDA requires, or the post-approval commitments that must be agreed to prior to approval; (iii) issue a not approvable letter which outlines steps required for approval, but which are typically more onerous than those in an approvable letter, and may require additional clinical studies that are often expensive and time consuming and can delay approval for months or even years; or (iv) deny the application. If the FDA issues an approvable or not approvable letter, the applicant has 180 days to respond, after which the FDA's review clock is reset.

The FDA will generally approve the new device for commercial distribution if it determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for its intended use(s). The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and collection of long-term follow-up data from patients in the clinical study that supported PMA approval or requirements to conduct additional clinical studies post-approval. The FDA may condition PMA approval on some form of post-market surveillance when deemed necessary to protect the public's health or to provide additional safety and efficacy data for the device in a larger population or for a longer period of use. In such cases, the manufacturer might be required to follow certain patient groups for a number of years and to make periodic reports to the FDA on the clinical status of those patients. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval.

Certain changes to an approved device, such as changes in manufacturing facilities, methods, or quality control procedures, or changes in the design performance specifications, which affect the safety or effectiveness of the device, require submission of a PMA supplement. PMA supplements often require submission of the same type of information as a PMA, except that the supplement is

limited to information needed to support any changes from the device covered by the original PMA and may not require as extensive clinical data or the convening of an advisory panel. Certain other changes to an approved device require the submission of a new PMA, such as when the design change causes a different intended use, mode of operation, and technical basis of operation, or when the design change is so significant that a new generation of the device will be developed, and the data that were submitted with the original PMA are not applicable for the change in demonstrating a reasonable assurance of safety and effectiveness.

Clinical Studies

Clinical studies are almost always required to support pre-market approval and are sometimes required for 510(k) clearance. All clinical investigations of investigational devices designed to determine safety and effectiveness must be conducted in accordance with the FDA's IDE regulations, which govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk" to human health, as defined by the FDA, the FDA requires the device sponsor to submit an IDE application to the FDA, which must become effective prior to commencing human clinical studies. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE will automatically become effective 30 days after receipt by the FDA unless the FDA notifies the company that the investigation may not begin. If the FDA determines that there are deficiencies or other concerns with an IDE for which it requires modification, the FDA may permit a clinical study to still proceed under a conditional approval. Acceptance of an IDE for review does not guarantee that the FDA will allow the IDE to become effective and, if it does become effective, the FDA may or may not determine that the data derived from the trials support the safety and effectiveness of the device or warrant the continuation of clinical studies.

Regardless of the degree of risk presented by the medical device, clinical studies must be approved by, and conducted under the oversight of, an IRB, for each clinical study site. An IRB is an appropriately constituted group that has been formally designated to review and monitor medical research involving subjects and which has the authority to approve, require modifications in, or disapprove research to protect the rights, safety and welfare of human research subjects. If an IDE application is approved by the FDA and one or more IRBs, human clinical studies may begin at a specific number of investigational sites with a specific number of patients, as approved by the FDA. If the evaluation of the device presents a non-significant risk to the patient, a sponsor may begin the clinical study after obtaining approval for the trial by one or more IRBs without separate approval from the FDA. However, the clinical study must still be conducted in compliance with abbreviated IDE requirements, such as monitoring the investigation, ensuring that the investigators obtain informed consent, and labeling and recordkeeping requirements. During a study, the sponsor is required to comply with the applicable FDA requirements, including, for example, trial monitoring, selecting clinical investigators and providing them with the investigational plan, ensuring IRB review, adverse event reporting, recordkeeping, and prohibitions on the promotion of investigational devices or on making safety or effectiveness claims for them. The clinical investigators in the clinical study are also subject to FDA regulations and must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and recordkeeping requirements. Additionally, after a trial begins, the sponsor, the FDA or the IRB could suspend or terminate a clinical study at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits, or failures to follow applicable regulations.

Sponsors of certain clinical studies of medical devices are required to register with clinicaltrials.gov, a public database of clinical study information. Information related to the device, patient population, phase of investigation, study sites and investigators and other aspects of the clinical study is made public as part of the registration.

Breakthrough Devices Program

Following passage of the 21st Century Cures Act, the FDA implemented the Breakthrough Devices Program, which is a voluntary program offered to manufacturers of certain medical devices and device-led combination products that may provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The goal of the program is to provide patients and healthcare providers with more timely access to qualifying devices by expediting their development, assessment and review, while preserving the statutory standards for PMA approval, 510(k) clearance and de novo classification. The program is

available to medical devices that meet certain eligibility criteria, including that the device provides more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, and that the device meets one of the following criteria: (i) the device represents a breakthrough technology, (ii) no approved or cleared alternatives exist, (iii) the device offers significant advantages over existing approved or cleared alternatives, or (iv) the availability of the device is in the best interest of patients. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of post-market data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions.

Ongoing Regulation by the FDA

Even after a device receives clearance or approval and is placed on the market, numerous regulatory requirements apply. These include:

- establishment registration and device listing;
- the QSR, which requires manufacturers, including third-party manufacturers, to follow stringent design, testing, control, documentation and other quality assurance procedures during all aspects of the manufacturing process;
- labeling regulations, which require that promotion is truthful, not misleading, fairly balanced, provides adequate directions for use, and that all claims are substantiated, and the FDA prohibitions against the promotion of products for uncleared, unapproved or “off-label” uses and other requirements related to promotional activities;
- medical device reporting regulations, which require that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury, or if their device malfunctioned and the device or a similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur;
- corrections and removal reporting regulations, which require that manufactures report to the FDA field corrections or removals if undertaken to reduce a risk to health posed by a device or to remedy a violation of the FDCA that may present a risk to health;
- complying with federal laws and regulations requiring Unique Device Identifiers on devices and also requiring the submission of certain information about each device to the FDA’s Global Unique Device Identification Database;
- the FDA’s recall authority, whereby the FDA can order device manufacturers to recall a medical device from the market if the FDA finds that there is a reasonable probability that the device would cause serious, adverse health consequences or death; and
- post-market surveillance regulations, which apply to certain Class II or Class III devices when necessary to protect the public’s health or to provide additional safety and effectiveness data for the device.

Manufacturing of medical devices is required to comply with the applicable portions of the QSR, which cover the methods and the facilities, controls for the design, manufacture, testing, production, processes, controls, quality assurance, labeling, packaging, distribution, installation, and servicing of finished devices intended for human use. The QSR also requires, among other things, maintenance of a device master file, device history file, and complaint files. As a manufacturer, our facilities, records, and manufacturing processes are subject to periodic scheduled or unscheduled inspections by the FDA. Our failure to maintain compliance with the QSR or other applicable regulatory requirements could result in the shut-down of, or restrictions on, its manufacturing operations and the recall or seizure of its products. The discovery of previously unknown problems with any marketed products, including unanticipated adverse events or adverse events of increasing severity or frequency, whether resulting from the use of the device within the scope of its clearance or off-label by a physician in the practice of medicine, could result in restrictions on the device, including the removal of the product from the market or voluntary or mandatory device recalls.

The FDA has broad regulatory compliance and enforcement powers. If the FDA determines that a manufacturer has failed to comply with applicable regulatory requirements, it can take a variety of compliance or enforcement actions, which may result in any of the following sanctions:

- warning or untitled letters, fines, injunctions, consent decrees and civil penalties;
- customer notifications, voluntary or mandatory recall or seizure of products;
- operating restrictions, partial suspension or total shutdown of production;
- refusals or delays in processing submissions or applications for new products or modifications to existing products;
- refusal to grant export or import approvals for products;
- withdrawing approvals that have already been granted; and
- criminal prosecution.

European Union

We believe our Virtue SAB, BackBeat CNT and CNT-HF product candidates as well as our FreeHold Devices would be regulated in the EU as medical devices.

The EU has adopted specific directives and regulations regulating the design, manufacture, clinical investigation, conformity assessment, labeling and adverse event reporting for medical devices (including active implantable medical devices).

Until May 25, 2021, medical devices (including active implantable medical devices) were regulated by Council Directive 93/42/EEC and Council Directive 90/385/EEC (the “EU Medical Devices Directives”), which have been repealed and replaced by the EU Medical Devices Regulation. Our current certificates have been granted under the EU Medical Devices Directives whose regimes are described below. However, as of May 26, 2021, some of the EU Medical Devices Regulation requirements apply in place of the corresponding requirements of the EU Medical Devices Directives with regard to registration of economic operators and of devices, post-market surveillance and vigilance requirements. If we want to market our medical devices in the EU, it will notably require that our devices be certified under the new regime set forth in the EU Medical Devices Regulation.

Medical Devices Directives

Under the EU Medical Devices Directives, all medical devices (including active implantable medical devices) placed on the market in the EU must meet the relevant essential requirements laid down in Annex I to the EU Medical Devices Directives, including the requirement that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performance intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. The European Commission has adopted various standards applicable to medical devices. These include standards governing common requirements, such as sterilization and safety of medical electrical equipment and product standards for certain types of medical devices. There are also harmonized standards relating to design and manufacture. While not mandatory, compliance with these standards is viewed as the easiest way to satisfy the essential requirements as a practical matter as it creates a rebuttable presumption that the device satisfies that essential requirement.

To demonstrate compliance with the essential requirements laid down in Annex I to the EU Medical Devices Directives, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. As a general rule, demonstration of conformity of medical devices and their manufacturers with the essential requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and

acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-assess the conformity of its products with the essential requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a notified body. Notified bodies are independent organizations designated by EU member states to assess the conformity of devices before being placed on the market. A notified body would typically audit and examine a product's technical dossiers and the manufacturers' quality system (the notified body must presume that quality systems which implement the relevant harmonized standards — which is ISO 13485:2016 for Medical Devices Quality Management Systems — conform to these requirements). If satisfied that the relevant product conforms to the relevant essential requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EU.

Throughout the term of the certificate of conformity, the manufacturer will be subject to periodic surveillance audits to verify continued compliance with the applicable requirements. In particular, there will be a new audit by the notified body before it will renew the relevant certificate(s).

Medical Devices Regulation

The regulatory landscape related to medical devices in the EU recently evolved. On April 5, 2017, the EU Medical Devices Regulation was adopted with the aim of ensuring better protection of public health and patient safety. The EU Medical Devices Regulation establishes a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. Unlike the EU Medical Devices Directives, the EU Medical Devices Regulation is directly applicable in EU member states without the need for member states to implement into national law. This aims at increasing harmonization across the EU.

The EU Medical Devices Regulation became effective on May 26, 2021. The new regulation, among other things:

- strengthens the rules on placing devices on the market (e.g., reclassification of certain devices and wider scope than the EU Medical Devices Directives) and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- establishes explicit provisions on importers' and distributors' obligations and responsibilities;
- imposes an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;
- sets up a central database (Eudamed) to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo a clinical evaluation consultation procedure by experts before they are placed on the market.

Devices lawfully placed on the market pursuant to the EU Medical Devices Directives prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025, provided that the requirements of the transitional provisions are fulfilled. In particular, the certificate in question must still be valid. However, even in this case, manufacturers must

comply with a number of new or reinforced requirements set forth in the EU Medical Devices Regulation, in particular the obligations described below.

The EU Medical Devices Regulation requires that before placing a device, other than a custom-made device, on the market, manufacturers (as well as other economic operators such as authorized representatives and importers) must register by submitting identification information to the electronic system (Eudamed), unless they have already registered. The information to be submitted by manufacturers (and authorized representatives) also includes the name, address and contact details of the person or persons responsible for regulatory compliance. The new regulation also requires that before placing a device, other than a custom-made device, on the market, manufacturers must assign a unique identifier to the device and provide it along with other core data to the unique device identifier ("UDI") database. These new requirements aim at ensuring better identification and traceability of the devices. Each device — and as applicable, each package — will have a UDI composed of two parts: a device identifier ("UDI-DI") specific to a device, and a production identifier ("UDI-PI") to identify the unit producing the device. Manufacturers are also notably responsible for entering the necessary data on Eudamed, which includes the UDI database, and for keeping it up to date. The obligations for registration in Eudamed will become applicable at a later date (as Eudamed is not yet fully functional). Until Eudamed is fully functional, the corresponding provisions of the EU Medical Devices Directive continue to apply for the purpose of meeting the obligations laid down in the provisions regarding exchange of information, including, and in particular, information regarding registration of devices and economic operators.

All manufacturers placing medical devices on the market in the EU must comply with the EU medical device vigilance system which has been reinforced by the EU Medical Devices Regulation. Under this system, serious incidents and Field Safety Corrective Actions ("FSCAs") must be reported to the relevant authorities of the EU member states. These reports will have to be submitted through Eudamed — once functional — and aim to ensure that, in addition to reporting to the relevant authorities of the EU member states, other actors such as the economic operators in the supply chain will also be informed. Until Eudamed is fully functional, the corresponding provisions of the EU Medical Devices Directives continue to apply. A serious incident is defined as any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect, which, directly or indirectly, might have led or might lead to the death of a patient or user or of other persons or to a temporary or permanent serious deterioration of a patient's, user's or other person's state of health or a serious public health threat. Manufacturers are required to take FSCAs defined as any corrective action for technical or medical reasons to prevent or reduce a risk of a serious incident associated with the use of a medical device that is made available on the market. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its legal representative to its customers and/or to the end users of the device through Field Safety Notices. For similar serious incidents that occur with the same device or device type and for which the root cause has been identified or a FSCA implemented or where the incidents are common and well documented, manufacturers may provide periodic summary reports instead of individual serious incident reports.

The advertising and promotion of medical devices is subject to some general principles set forth in EU legislation. According to the EU Medical Devices Regulation, only devices that are CE-marked may be marketed and advertised in the EU in accordance with their intended purpose. Directive 2006/114/EC concerning misleading and comparative advertising and Directive 2005/29/EC on unfair commercial practices, while not specific to the advertising of medical devices, also apply to the advertising thereof and contain general rules, for example, requiring that advertisements are evidenced, balanced and not misleading. Specific requirements are defined at a national level. EU member states' laws related to the advertising and promotion of medical devices, which vary between jurisdictions, may limit or restrict the advertising and promotion of products to the general public and may impose limitations on promotional activities with healthcare professionals.

Many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medical devices, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on medical device manufacturers. Certain countries also mandate implementation of commercial compliance programs.

The aforementioned EU rules are generally applicable in the EEA, which consists of the 27 EU Member States plus Norway, Liechtenstein and Iceland.

United Kingdom

In the United Kingdom ("UK"), the medical devices market is regulated by the Medicines and Healthcare products Regulatory Agency ("MHRA"), which performs market surveillance of medical devices on the UK market. Devices are regulated under the Medical Devices Regulations 2002, which gave effect in UK law to the following EU directives: Directive 90/385/EEC on active implantable medical device; Directive 93/42/EEC on medical devices; and Directive 98/79/EC on in vitro diagnostic medical devices. The UK Conformity Assessed ("UKCA") marking is a UK product marking used for medical devices being placed on the Great Britain market. It is not recognized in the EU, so these products require a CE marking as well. CE marketed devices will be accepted on the Great Britain market until June 30, 2023. From July 1, 2023, devices placed on the Great Britain market will need to conform to UKCA marketing requirements.

We may need to support clinical and/or regulatory requirements in the UK for its BackBeat CNT product candidate, and potentially others.

Other Regions

Most major markets have different levels of regulatory requirements for medical devices. Modifications to the approved or certified products may require a new regulatory submission in all major markets. The regulatory requirements, and the review time, vary significantly from country to country. Products can also be marketed in other countries that have minimal requirements for medical devices.

Drug Regulation

United States

In the United States, our SirolimusEFR product candidate is subject to extensive regulation by the FDA, which regulates drugs under the FDCA and its implementing regulations, and other federal, state, and local regulatory authorities. The process of obtaining regulatory approvals and certifications and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's Good Laboratory Practice regulations;
- submission to the FDA of an IND application, which must become effective before human clinical studies may begin;
- approval by an independent IRB or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical studies in accordance with GCP requirements to establish the safety and efficacy of the proposed drug product for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data;

- payment of user fees; and

- FDA review and approval of the NDA.

We have performed CMC testing in support of our IDE approval for the combination product Virtue SAB that includes populating a DMF. We intend to follow up post-IDE approval for the Virtue SAB with exploring additional pre-clinical work to support additional indications. Depending on the indication, we may be able to leverage some of the biocompatibility and CMC data in the DMF, while providing additional data depending on the indication selected.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective and a clinical study proposed in the IND may begin 30 days after the FDA receives the IND, unless before that time the FDA raises concerns or questions related to one or more proposed clinical studies and places the clinical study on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. As a result, submission of an IND may not result in the FDA allowing clinical studies to commence.

We believe that additional preclinical studies will be necessary for evaluating SirolimusEFR in new indications (either as a combination product or a drug product).

Clinical Studies

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IRB at each institution participating in the clinical study must review and approve the plan for any clinical study before it commences at that institution, and the IRB must continue to oversee the clinical study while it is being conducted. Some trials also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a Data Safety Monitoring Board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical study if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Information about certain clinical studies must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their *www.clinicaltrials.gov* website.

Human clinical studies are typically conducted in three or four sequential phases, which may overlap or be combined:

- *Phase 1*: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- *Phase 2*: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3*: The drug is administered to an expanded patient population, generally at geographically dispersed clinical study sites, in well-controlled clinical studies to generate enough data to statistically evaluate the efficacy and safety of the product

for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- *Phase 4*: In some cases, the FDA may conditionally approve an NDA for a product candidate on the sponsor's agreement to conduct additional clinical studies after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical studies post-approval to gain more information about the drug. Certain post-approval trials may be typically referred to as Phase 4 clinical studies.

Progress reports detailing the results of the clinical studies, among other information, must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Furthermore, the FDA or the sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk or the failure to meet the trial's objectives. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

We believe that additional clinical studies will be necessary for evaluating SirolimusEFR in new indications (either as a combination product or a drug product).

Marketing Approval

Assuming successful completion of the required clinical testing in accordance with all applicable regulatory requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act ("PDUFA") guidelines that are currently in effect, the FDA has a goal of 10 months to review and act on an NDA designed for standard review and six months to review and act on an NDA designed for priority review, measured from the "filing" date for an NDA for a new molecular entity ("NME") or from the receipt date for an NDA for a non-NME product. Measuring from the "filing" date typically adds approximately two months to the timeline for review and decision, because the FDA has sixty days from receipt to make a "filing" decision, as described below.

In addition, under the Pediatric Research Equity Act of 2003 as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a REMS plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical study sites to assure compliance with GCP requirements.

The FDA generally accepts data from foreign clinical studies in support of an NDA if the trials were conducted under an IND. If a foreign clinical study is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an on-site inspection, if deemed necessary. The FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical study sites, if any, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter generally contains a statement of specific conditions that must be met to secure final approval of the NDA and may require additional clinical testing, preclinical testing, manufacturing or formulation modifications or other changes in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical studies, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

SirolimusEFR is the drug product component of our combination product Virtue SAB. We have yet to receive IDE approval for Virtue SAB.

The Hatch-Waxman Amendments

Our current regulatory strategy is to pursue development of its standalone SirolimusEFR product candidate for potential indications such as ophthalmic inflammatory conditions (uveitis) and chronic joint inflammation (osteoarthritis) as a Section 505(b)(2) NDA. As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on the FDA's previous findings of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by or for the applicant and for which the applicant does not contain a right of reference. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the product candidate. The FDA may also require companies to perform

additional studies or measurements, including clinical studies, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the branded reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Orange Book Listing

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, known as the Orange Book. Any applicant who files an Abbreviated New Drug Application ("ANDA") seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify, for each patent listed in the Orange Book for the referenced drug, to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) the date on which such patent expires or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. The fourth certification described above is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. This section viii statement does not require notice to the patent holder or NDA owner. There might also be no relevant patent certification.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the applicant. Even if the 45 days expire, a patent infringement lawsuit can be brought and could delay market entry, but it would not extend the FDA-related 30-month stay of approval.

The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired. Specifically, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. During the five-year exclusivity period, the FDA cannot accept for filing and cannot approve any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that the FDA may accept an application for filing after four years (and may initiate a review of the application, but still may not approve it for five years) if the follow-on applicant makes a paragraph IV certification. This exclusivity period may be extended by an additional six months if certain requirements are met to qualify the product for pediatric exclusivity, including the receipt of a written request from the FDA that the NDA holder conduct certain pediatric studies, the submission of study reports from such studies to the FDA after receipt of the written request and satisfaction of the conditions specified in the written request.

In addition, a drug, including one approved under Section 505(b)(2), may also obtain a three-year period of market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application that relies on the information supporting the approval of the drug, or the change to the drug for which the information was submitted and the exclusivity granted, until after that three-year exclusivity period has run. However, unlike for NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA and other government authorities, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most

changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to prior FDA review and approval. There also are continuing annual program fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical studies, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state authorities and are subject to periodic unannounced inspections by the FDA and these state authorities for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution or other restrictions under a REMS program.

Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on ongoing or proposed clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. A company can make only those claims that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional

conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (the "PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical studies and commercial sales and distribution of its products. Whether or not we obtain FDA approval for a product, it must obtain approval or certification by the comparable regulatory authorities of foreign countries before it can commence clinical studies, and approval or certification from regulatory authorities in foreign countries, such as the EU, before it may market products in those countries. The requirements and process governing the conduct of clinical studies, approval process, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical studies

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice ("GLP") as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical studies of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization's ("ICH") GCPs, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical study is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical study insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical study.

The regulatory landscape related to clinical study in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR"), which was adopted in April 2014 and repeals the EU Clinical Trials Directive (the "Clinical Trials Directive"), became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical studies throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical studies will be governed by the CTR varies. For clinical studies whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical studies must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MA" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Product for Human Use ("CHMP") of the EMA and are valid throughout the EU. The centralized procedure is mandatory for certain types of product candidates, such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicines, (iii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases and (iv) advanced therapy medicinal products ("ATMPs") such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days.

In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical study designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are

provided, it can become a “standard” MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted “under exceptional circumstances” when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA “under exceptional circumstances” is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Data and marketing exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical study data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU’s regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (“PSURs”).

All new MAAs must include a risk management plan (“RMP”) describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical studies or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

Failure to comply with EU and member state laws that apply to the conduct of clinical studies, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative,

civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical studies, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical studies, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Regulation of Combination Products in the EU

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework.

Drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. The EMA is responsible for evaluating the quality, safety and efficacy of MAAs submitted through the centralized procedure, including the safety and performance of the medical device in relation to its use with the medicinal product. The EMA or the EU member state national competent authority will assess the product in accordance with the rules for medicinal products described above but the device part must comply with the EU Medical Devices Regulation (including the general safety and performance requirements provided in Annex I). The MAA must include — where available — the results of the assessment of the conformity of the device part with the Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the competent authority must require the applicant to provide a notified body opinion on the conformity of the device.

By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the EU Medical Devices Regulation.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product.

The requirements regarding quality documentation for medicinal products when used with a medical device, including single integral products, co-packaged and referenced products, are outlined in the EMA guideline of July 22, 2021, which became applicable as of January 1, 2022.

The aforementioned EU rules are generally applicable in the EEA.

Coverage and Reimbursement

Sales of any pharmaceutical and medical device product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for medical devices, pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical devices and pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Fraud and Abuse and Other Healthcare Regulations

Federal and state governmental agencies and equivalent foreign authorities subject the healthcare industry to intense regulatory scrutiny, including heightened civil and criminal enforcement efforts. These laws constrain the sales, marketing and other promotional activities of medical device manufacturers by limiting the kinds of financial arrangements we may have with hospitals, physicians and other potential purchasers of its products. Federal healthcare fraud and abuse laws apply to our business when a customer submits a claim for an item or service that is reimbursed under Medicare, Medicaid or other federally funded healthcare programs. Patient privacy statutes and regulations by foreign, federal and state governments may also apply in the locations in which we do business. Descriptions of some of the U.S. laws and regulations that may affect our ability to operate follow.

Federal Healthcare Anti-Kickback Statute

The federal Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value, and the government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the law or a specific intent to violate it. In addition, the government may assert that a claim, including items or services resulting from a violation of the Anti-Kickback Statute, constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The Anti-Kickback Statute is subject to evolving interpretations and has been applied by government enforcement officials to a number of common business arrangements in the medical device industry. There are a number of statutory exceptions and regulatory safe harbors protecting certain business arrangements from prosecution under the Anti-Kickback Statute; however, those exceptions and safe harbors are drawn narrowly and there is no exception or safe harbor for many common business activities, such as reimbursement support programs, educational and research grants or charitable donations. The failure of a transaction or arrangement to fit precisely within one or more applicable statutory exceptions or regulatory safe harbors does not necessarily mean that it is illegal or that prosecution will be pursued. However, conduct and business arrangements that do not fully satisfy all requirements of an applicable safe harbor may result in increased scrutiny by government enforcement authorities and will be evaluated on a case-by-case basis based on a cumulative review of all facts and circumstances.

Federal Civil False Claims Act

The federal civil False Claims Act prohibits, among other things, persons or entities from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to be made or used a

false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government. A claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Actions under the federal civil False Claims Act may be brought by the government or as a qui tam action by a private individual in the name of the government. These individuals, sometimes known as "relators" or, more commonly, as "whistleblowers," may share in any amounts paid by the entity to the government in fines or settlement. The number of filings of qui tam actions has increased significantly in recent years. Qui tam actions are filed under seal and impose a mandatory duty on the U.S. Department of Justice to investigate such allegations. Most private citizen actions are declined by the Department of Justice or dismissed by federal courts. However, the investigation costs for a company can be significant and material even if the allegations are without merit. Various states have adopted laws similar to the federal civil False Claims Act, and many of these state laws are broader in scope and apply to all payors, and therefore, are not limited to only those claims submitted to the federal government. Medical device manufacturers and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

Healthcare Fraud Statute

HIPAA and its implementing regulations created federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Sunshine Act

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually with certain exceptions to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (as defined by statute), certain non-physician practitioners, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives, and teaching hospitals, either directly or indirectly through a third party at the request of such physician, non-physician practitioner or teaching hospital, as well as ownership and investment interests held by physicians and their immediate family members.

Other State Laws

Certain states also mandate implementation of commercial compliance programs, impose restrictions on device manufacturer marketing practices and/or require tracking and reporting of gifts, compensation and other remuneration to healthcare professionals and entities.

State and federal regulatory and enforcement agencies continue to actively investigate violations of healthcare laws and regulations, and the U.S. Congress continues to strengthen the arsenal of enforcement tools. The Bipartisan Budget Act of 2018 (the "BBA") increased the criminal and civil penalties that can be imposed for violating certain federal healthcare laws, including the Anti-Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular, government agencies recently have increased regulatory scrutiny and enforcement activity with respect to manufacturer reimbursement support activities and other patient support programs, including bringing criminal charges or civil enforcement actions under the Anti-Kickback Statute, federal civil False Claims Act and violations of healthcare fraud and HIPAA privacy provisions.

Enforcement and Penalties for Noncompliance with Fraud and Abuse Laws and Regulations

Compliance with these federal and state laws and regulations requires substantial resources. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to it, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from participation in government healthcare programs such as the Medicare and Medicaid programs, reputational harm, administrative burdens, diminished profits and

future earnings, and the curtailment or restructuring of its operations. Companies settling federal civil False Claims Act, Anti-Kickback Statute and other fraud and abuse cases also may be required to enter into a Corporate Integrity Agreement with the U.S. Department of Health and Human Services Office of Inspector General in order to avoid exclusion from participation (*i.e.*, loss of coverage for their products) in federal healthcare programs such as Medicare and Medicaid. Corporate Integrity Agreements typically impose substantial costs on companies to ensure compliance.

For additional information regarding obligations under federal healthcare statues and regulations, please see the section titled "*Risk Factors — Risks Related to Government Regulation and Our Industry — Our relationships with physicians, patients and payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, and other healthcare laws and regulations*."

United States Healthcare Reform

There have been and continue to be proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of healthcare and, more generally, to reform the U.S. healthcare system.

For example, in the United States, in March 2010, the ACA, was enacted. The ACA contained a number of significant provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which impacted existing government healthcare programs and resulted in the development of new programs. The ACA also imposed an excise tax of 2.3% on the sale of most medical devices, which was suspended, effective January 1, 2016, and subsequently repealed, effective January 1, 2020.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, includes reductions to Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2031, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to bring transparency to product pricing and reduce the cost of products and services under government healthcare programs. Additionally, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what products to purchase and which suppliers will be included in their healthcare programs.

We expect additional state, federal and foreign healthcare reform measures to be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure.

For instance, in December 2021, the EU Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. This regulation which entered into force in January 2022 intends to boost cooperation among EU member states in assessing health technologies, including some medical devices, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of

our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Our Employees

As of October 6, 2023, we had 56 employees engaged in finance, clinical, research and development, engineering, regulatory and administration functions. We anticipate that the number of employees will grow as we scale our research and development and clinical organizational capabilities. In addition, we utilize and will continue to utilize consultants, clinical research organizations and third parties to perform our analytical and test method development, component and sub-assembly design and manufacturing, as well as preclinical studies, clinical studies, manufacturing and regulatory functions. We will use consultants and third-party analytical and design houses to complement internal capabilities and will utilize external manufacturing partners that have extensive experience in medical devices and dealing with regulatory bodies to provide components, assemblies and final product. Our suppliers will have ISO 13485 approved quality systems (or have been approved for GMP manufacturing of pharmaceutical products).

None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our employee relations to be good.

Our Facilities

We are the lessee of 5,461 square feet of office and laboratory space in New Hope, Pennsylvania. In January 2019, we signed a lease extension which added an additional 2,591 square feet to our existing lease. The new lease totals approximately 8,052 square feet and began in October 2019 and expires five years later in September 2024 at an annual rental of approximately $209,230. The laboratories support research, development and analytical functions of both formulation and device components of Virtue SAB. We will use these laboratories to perform all non-GMP analytical methods related to formulation characterization and release specifications (high performance liquid chromatography, dynamic light scattering, light obscuration, thermal analysis, etc.) as well as pilot scale production of formulation. We will also conduct engineering and device testing (burst, compliance, flow, dose delivery) and method development for Virtue SAB in this facility.

In November 2019, we entered into a lease agreement for approximately 5,200 square feet of office space in New York, New York. The lease will expire in March 2028. The monthly lease payments commenced five months after the date of the agreement. Simultaneously, as stipulated in the lease agreement, we obtained and delivered an unconditional, irrevocable letter of credit of approximately $336,000 from a financial institution, which expires in October 2023.

In January 2020, we entered into an agreement for the use of portions of the premises of Motus GI, a related party, for office space in Fort Lauderdale, Florida. The agreement will expire in November 2024. The monthly fee commenced on the month following the date of the agreement. Monthly fees will be between approximately $7,000 and $23,000 for the period from commencement through termination. The amount paid is estimated to be proportionate to the percentage of space used by us applied to the monthly rent obligated to be paid by Motus GI to its landlord. As noted above, we currently have a minority equity interest in Motus GI and own a royalty certificate that entitles us to certain royalty payments from Motus GI. In addition, Mr. Hochman, our chief executive officer, served as Chairman of the board of directors of Motus GI from December 2016 to April 2023, and remained as a member of the board of directors until September 2023. Mr. Sherman, our president and chief operating officer, also served on the board of directors of Motus GI from December 2016 to September 2023.

Legal Proceedings

We are not currently subject to any material legal proceedings. We may be subject to other legal proceedings and claims in the ordinary course of business. We cannot predict the results of any such disputes, and despite the potential outcomes, potential legal proceedings and claims may have an adverse material impact on it due to diversion of management time and attention as well as the financial costs related to resolving such disputes.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the name, age and position of each of our directors, executive officers and certain key executives. For biographical information concerning the directors, executive officers and key executives, see below.

Name	Age[1]	Position
Executive Officers and Directors		
David P. Hochman	48	Chief Executive Officer, Chairman of the Board and Director
Darren R. Sherman	52	President, Chief Operating Officer and Director
Yuval Mika, Ph.D.	65	General Manager and Chief Technology Officer, Bioelectronic Therapies
George Papandreou, Ph.D.	58	General Manager and Senior Vice President, Focal Therapies
Andrew L. Taylor	52	Chief Financial Officer
William R. Little	52	Executive Vice President, Corporate Development & Strategy
Non-Executive Directors		
Jason Aryeh[2][4]	55	Director
Pamela A. Connealy[2]	62	Director
Eric S. Fain, M.D.[3][4]	63	Lead Director
Eric A. Rose, M.D.[3][4]	72	Director
Geoffrey W. Smith[2][3]	58	Director

(1) As of October 6, 2023.
(2) Member of Audit Committee
(3) Member of Compensation Committee
(4) Member of Nominating and Corporate Governance Committee

Executive Officers

David P. Hochman — Chief Executive Officer, Chairman of the Board and Director

Mr. Hochman has served as the Chairman of our Board and as our Chief Executive Officer since the closing of the Business Combination in January 2023. From May 2018 to the closing of the Business Combination, he served as Legacy Orchestra's Chief Executive Officer and Chairman of the Legacy Orchestra board of directors ("Legacy Orchestra Board"). He also co-founded Legacy Orchestra and its predecessors, which predecessors are now our wholly-owned subsidiaries, Caliber, BackBeat and FreeHold. Mr. Hochman served as a member of the boards of directors of Caliber, FreeHold and BackBeat from December 2008, December 2010 and June 2010, respectively, until November 2018. He also served as BackBeat's President from its inception in June 2010 until May 2018. Mr. Hochman has served as a board observer of Vivasure since 2019. Mr. Hochman has over 25 years of healthcare entrepreneurial, venture capital and investment banking experience. From 2006 until December 2019, he co-founded and was Managing Partner of Orchestra Medical Ventures, LLC ("OMV"), a medical technology venture capital firm. Funds managed by OMV were stockholders of Orchestra prior to their dissolution. From December 2009 to until its purchase by Legacy Orchestra in December 2019, Mr. Hochman served as President and a board member of Accelerated Technologies, Inc., a medical device accelerator company managed by OMV that helped create the concepts for BackBeat CNT, Virtue SAB, FreeHold Devices, the Pure-Vu system, PerQSeal. From December 2016 to September 2023, Mr. Hochman served as a member of the board of directors of Motus GI (Nasdaq: MOTS), a Nasdaq-listed medical technology company in which Orchestra has a strategic investment, from December 2016 to September 2023 and as its Chairman of the Board from December 2016 to April 2023. From December 2013 until September 2020, Mr. Hochman was a co-founder and board member of Corbus Pharmaceuticals Holdings, Inc. (Nasdaq: CRBP), a Nasdaq-listed clinical stage biopharmaceutical company. Prior to co-founding OMV, Mr. Hochman was Chief Executive Officer of Spencer Trask Edison Partners, LLC, an investment partnership focused on early stage healthcare companies, from 2002 to 2006. He was also Managing Director of private equity firm Spencer Trask Ventures, Inc. from 2000 to 2006, during which time he led financing transactions for over twenty early-stage companies raising over $420.0 million. From 1999 to 2006, Mr. Hochman was a board advisor of Health Dialog Services Corporation, a leader in collaborative healthcare management that was acquired in 2008 by the British United Provident Association for $750.0 million. From 2005 to 2007, he was a co-founder and board member of PROLOR

Biotech, Inc., a formerly NYSE-listed biopharmaceutical company developing longer lasting versions of approved therapeutic proteins, which was purchased by Opko Health, Inc. in 2013 for over $600.0 million. He currently serves as President and a board member of the Mollie Parnis Livingston Foundation. He earned a B.A. with honors from the University of Michigan.

We believe that Mr. Hochman's role as a co-founder of Legacy Orchestra's predecessors and founder of Legacy Orchestra, his experience in healthcare innovation and venture capital, his leadership at other companies, including publicly-traded medical technology and biotechnology companies, his financial experience, and his extensive knowledge of our business based on his years as Chief Executive Officer provide him with the qualifications and skills to serve on our Board.

Darren R. Sherman — President, Chief Operating Officer, Director and Founder

Mr. Sherman has served as President and Chief Operating Officer and a member of our Board since the closing of the Business Combination in January 2023. From May 2018 to the closing of the Business Combination, he served as Legacy Orchestra's President and Chief Operating Officer and a member of the Legacy Orchestra Board. He also co-founded Legacy Orchestra and its predecessors, which predecessors are now our wholly-owned subsidiaries, Caliber, BackBeat and FreeHold. Mr. Sherman served as Chief Executive Officer of Caliber from 2009 to May 2018 and as Chief Executive Officer and President of FreeHold from 2012 to May 2018. He also served as a board member of Caliber, FreeHold and BackBeat from 2009, 2012 and 2010, respectively, until November 2018. From 2009 until December 2019, Mr. Sherman was Managing Partner of OMV, a medical technology venture capital firm. Funds managed by OMV were stockholders of Orchestra prior to their dissolution. From 2009 to December 2019, Mr. Sherman also served as Chief Technical Officer of Accelerated Technologies, Inc., a medical device accelerator company managed by OMV that Orchestra acquired in December 2019. Mr. Sherman has over 25 years of management and entrepreneurial experience in the medical technology industry spanning interventional cardiology, cardiac electrophysiology, sudden cardiac death, stroke, surgery, GI, and neurovascular therapies. From 2009 until August 2016, he served on the board of directors of Vivasure, in which Orchestra holds a strategic investment. He served as a director of Motus GI (Nasdaq: MOTS), a Nasdaq-listed medical technology company that Orchestra also has a strategic holding in, from December 2016 to September 2023. Prior to joining OMV, from February 2002 until March 2008, Mr. Sherman held various positions in executive management for Cordis Neurovascular, a Johnson & Johnson company that focused on leveraging technology into applications for the brain, including Executive Director of Research & Development and Director of Strategic Marketing. From January 1997 until February 2002, Mr. Sherman played an integral role in the formation and development of Revivant Corp., a company that designs, manufactures, and markets AutoPulse and medical devices that automate cardiopulmonary resuscitation, prior to its acquisition by Zoll Medical Corporation, while working with Thomas J. Fogarty, M.D. at Fogarty Engineering Inc. From January 1995 until January 1997, Mr. Sherman held positions in research and development for Cardiac Pathways Corp., which manufactured minimally-invasive systems used to diagnose and treat cardiac tachyarrhythmias prior to its acquisition by Boston Scientific. Prior to Cardiac Pathways Corp., he worked at Baxter Healthcare, a healthcare company specializing in medical devices, pharmaceuticals and biotechnology. Mr. Sherman has authored more than 85 U.S. patents with an additional 100+ published applications. He earned a B.S. in Bioengineering from the University of California, San Diego. We believe that Mr. Sherman's role as a co-founder of Legacy Orchestra's predecessors and founder of Legacy Orchestra, his experience in medical device innovation, his leadership at other companies, including medical technology companies, his product development experience, and his extensive knowledge of our business provide him with the qualifications and skills to serve on our Board.

Yuval Mika, Ph.D. — General Manager and Chief Technology Officer, Bioelectronic Therapies

Dr. Mika has served as the General Manager and Chief Technology Officer of our Bioelectronic Therapies group since January 2023. Prior to that, he served in the same role at Legacy Orchestra since May 2018. Between June 2011 and May 2018, Dr. Mika served as the Chief Executive Officer of BackBeat, one of Legacy Orchestra's predecessors and now a wholly-owned subsidiary, and previously served as a consultant to BackBeat from February 2010 to June 2011. He was one of the founders of BackBeat and the leader in the development of BackBeat Cardiac Neuromodulation Therapy from concept and design through preclinical and clinical work demonstrating the effect of the therapy in lowering blood pressure. Dr. Mika has over 25 years of experience in the medical device industry, bringing technologies from concept to commercialization. He has managed the development of active implantable devices for the treatment of major diseases, including heart failure, obesity and diabetes. Dr. Mika started his career in 1992 as a leading researcher at Carmel Biotechnology Ltd. in Israel (later called Carmel Biosensors), a developer of diagnostics of diabetes, where he developed an implantable biosensor for continued measurement of glucose. In 1996, Dr. Mika became the Chief Scientist and one of the founders of Impulse Dynamics, a medical device company developing an implantable cardiac stimulator for the treatment of heart failure. In 1998, Dr. Mika became Impulse Dynamics' Vice President of Research and Development and was responsible for the development as well as preclinical and clinical evaluation of the company's implantable system. Dr. Mika was part

of the team that secured an option agreement, receiving $250.0 million in cash from Johnson & Johnson and Guidant Corporation for the option to acquire Impulse Dynamics' technology. In 2001, Dr. Mika was appointed the General Manager of Impulse Dynamics and managed the initial clinical studies of the company and the CE approval of its device and cardiac contractility modulation therapy in Europe. In 2005, Dr. Mika was appointed as the Chief Operating Officer and acting Chief Executive Officer of Impulse Dynamics, leading the company's large-scale randomized studies in Europe and its IDE study in the United States, obtaining high value Diagnosis Related Group reimbursement to the system in Europe, reimbursement codes for the system in the United States and initiating the commercialization of the system in Europe. In 2003, Dr. Mika led the development of a bioelectrical therapy for the treatment of obesity and diabetes based on the concept of impulse dynamics therapy. This led to the formation of MetaCure, a developer of implantable devices for the treatment of obesity and diabetes. Dr. Mika served as MetaCure's Chief Operating Officer in 2005 and was the Chief Scientist of MetaCure until 2007. Dr. Mika earned a B.Sc in electrical engineering and a D.Sc in biophysics from the Technion — Israel Institute of Technology.

George Papandreou, Ph.D. — General Manager and Senior Vice President, Focal Therapies

Dr. Papandreou has served as the General Manager and Senior Vice President, of our Focal Therapies group since March 2023. Prior to that, he served as the Senior Vice President of Quality for Legacy Orchestra since July 2021. Dr. Papandreou is a global organizational leader with over 25 years in research and development, quality assurance, regulatory and general management experience. Between January 2017 and July 2021, he held positions of increased responsibilities at C.R. Bard/Becton Dickinson, including Vice President and Scientific Advisor, Vice President and Site Leader, Vice President Quality and Regulatory, and Vice President Quality. Prior to that, Dr. Papandreou worked for 17 years at Cordis Corporation, a Johnson & Johnson company, where he started as a Staff Scientist and completed his tenure as Senior Research Fellow with oversight for a team developing novel formulations for drug/device combination products. Dr. Papandreou holds a B.S. in Chemistry from the University of Athens, Athens, Greece and a Ph.D. in Organic Chemistry from Cornell University, Ithaca, New York.

Andrew L. Taylor — Chief Financial Officer

Mr. Taylor has served as our Chief Financial Officer since June 2023. Prior to joining, Mr. Taylor served as Chief Financial Officer of Motus GI (Nasdaq: MOTS) from August 2017 until June 2023. Mr. Taylor served as the CFO and President of Avertix Medical, Inc. (f/k/a Angel Medical Systems, Inc.) from 2007 until 2017 and has served on the board of directors of Avertix Medical since 2017. Avertix Medical is a medical device company that develops and manufactures ischemia monitoring and alerting systems. While at Avertix Medical, Mr. Taylor supervised the majority of the operations and employees in the United States and Brazil, while also overseeing the financial planning and analysis activities, capital raising and licensing efforts, and implementation of capital and operating budgets. From 2005 to 2007, Mr. Taylor was a Practice Leader for AC Lordi Consulting (now part of BDO USA, LLP), where he oversaw staff providing CFO and Controller consulting services. Prior to that, Mr. Taylor was the CFO of Safe3w, Inc. from 2001 to 2005 until its acquisition by iPass, Inc., where he led all accounting and finance functions as well as the fundraising efforts, and negotiated the sale of the company. From 1999 to 2001, Mr. Taylor served as the Vice President of Finance and Administration of Abridge, Inc., where he developed and managed processes for budgeting, forecasting and cash management. Prior to that, Mr. Taylor was a Senior Finance Associate at Delta Air Lines (NYSE: DAL), from 1998 to 1999. Mr. Taylor earned a B.A. in Political Science and Economics at McGill University and his MBA in Finance at Northeastern University, and is a CFA Program Level II Candidate.

On December 31, 2018, Angel Medical Systems, Inc. filed a voluntary petition for relief under Chapter 11 of Title 11 of the United States Bankruptcy Code in the U.S. Bankruptcy Court for the District of Delaware (the "Bankruptcy Court"). On February 11, 2019, the conditions of the Chapter 11 Plan of Reorganization (the "Bankruptcy Plan") for Angel Medical Systems, Inc. were confirmed by the Bankruptcy Court. On March 29, 2019, the Bankruptcy Plan became effective and Angel Medical Systems, Inc. emerged from its Chapter 11 reorganization as a private company.

William R. Little — Executive Vice President, Corporate Development & Strategy

Mr. Little has served as our Executive Vice President, Corporate Development & Strategy since June 2023. Prior to joining, Mr. Little served as Chief Operating Officer of Neovasc Inc. from November 2019 until its acquisition by Shockwave Medical, Inc. in April 2023. Mr. Little is an accomplished global marketing executive with more than two decades of experience in the medical device and technology spaces, specializing in interventional cardiology and structural heart disease. Prior to Neovasc, Mr. Little served as Head of Customer and New Market Insights and Divisional Vice President of Global Marketing for Abbott Laboratories ("Abbott") from January 2012 through November 2019, where he led strategy for the company's $3 billion vascular business unit. He also led

organizational integration during Abbott's $30 billion merger with St. Jude Medical, providing U.S. sales leadership for a 300-strong commercial field team. Prior to Abbott, Mr. Little was Vice President, Global Marketing at C.R. Bard, Inc. now part of Becton Dickinson, where he executed on a marketing strategy for the company's $600 million peripheral vascular franchise, completing 12 new product launches that generated total revenue in excess of $100 million annually. He also spent over 13 years at Boston Scientific in a variety of domestic and international commercial roles. Mr. Little also serves as a director and member of the HR committee of Medyria, a medtech company that engineers technologies for endovascular catheter navigation and sensing, and a director of SpectraWAVE, Inc.. a cardiology device company. Mr. Little holds a Bachelor of Science in business administration and marketing from the University of Colorado.

Non-Executive Directors

Jason Aryeh

Mr. Aryeh has served as a member of our Board since January 2023. Prior to that, he served as a director of Legacy Orchestra since November 2018. He previously served as a strategic advisor to Legacy Orchestra from July 2018 to November 2018. Mr. Aryeh is the founder and managing general partner of JALAA Equities, LP, a private investment fund focused on the biotechnology and medical device sectors, and has served in such capacity since 1997. Since September 2006, he has also served on the board of directors of Ligand Pharmaceuticals, Inc. (Nasdaq: LGND), a Nasdaq-listed biopharmaceutical company focused on developing or acquiring technologies that help pharmaceutical companies discover and develop medicines. He currently serves as Chairman of its Nominating and Governance Committee and has previously served as a member on its Compensation Committee. Since March 2021, Mr. Aryeh has also served on the board of directors of Anebulo Pharmaceuticals (Nasdaq: ANEB), a Nasdaq-listed biotechnology company, where he currently serves on the Audit Committee. Mr. Aryeh has also served as Executive Chair of Rio Grande Renewables, LLC, a renewable energy company he co-founded, since March 2009. He has served on the board of directors of multiple public and private life sciences companies since 2006, including Novelion Therapeutics Inc., which was a Nasdaq-listed biopharmaceutical company that focused on investing in science and clinical development of therapies for rare diseases, from November 2016 to August 2018, and its predecessor, QLT Inc., from June 2013 to November 2016. He also served on the Cystic Fibrosis Foundation's Therapeutics board of directors from 2012 to February 2019. Mr. Aryeh earned a B.A. in economics, with honors, from Colgate University.

We believe that Mr. Aryeh's finance background and extensive experience as a board member and an investor in life science companies, including his service as managing general partner of an investment fund focused on the life sciences sector and over 13 years as a board member of Ligand Pharmaceuticals, Inc., a leader in shared risk and reward partnering to drive innovation in the field of biopharmaceuticals, provide him with the qualifications and skills to serve on our Board.

Pamela Ann Connealy

Ms. Connealy has served as a member of our Board since January 2023. Prior to that, she served as a director of Legacy Orchestra since February 2020. She has a wealth of leadership experience in biotech finance, business operations, strategic planning and management. She is currently the Chief Financial Officer and Chief Operating Officer of Pyxis Oncology, Inc. (Nasdaq: PYXS), a clinical stage oncology company, where she has served in such capacity since July 2021. Prior to Pyxis Oncology, Ms. Connealy served as Chief Financial Officer and Chief Human Resources Officer of Immunovant, Inc. (Nasdaq: IMVT), a biotech company focused on transformative therapies for patients with autoimmune diseases, from November 2019 to September 2021. At Immunovant, Inc., Ms. Connealy led finance, investor relations and human resources. She also has served as an advisor to Perfuse Therapeutics, an early-stage company focused on ophthalmic diseases, since October 2019. Prior to Immunovant, Inc., from August 2018 to November 2019, Ms. Connealy served as Chief Financial Officer, Chief Operating Officer and Chief Human Resources Officer of Kiva Microfunds, a San Francisco-based nonprofit organization focused on expanding financial access for underserved communities. From April 2015 to June 2018, she served as Global Head of Talent at the Bill & Melinda Gates Foundation, a private foundation, where she focused on talent management, compensation, benefits and global mobility. From March 2012 to November 2013, she served as Vice President of Business Operations at Salesforce.com Inc., an enterprise software company, and from March 2002 to April 2010, she served as Vice President and Corporate Officer at Genentech, Inc., a biotechnology company focused on developing, manufacturing and commercializing medicines to treat patients with serious and life-threatening medical conditions, with roles including Chief Financial Officer of Research & Development, Head of Global Procurement and other key global operational roles. Ms. Connealy earned an M.B.A. in finance from the University of St. Thomas and a B.S. in chemistry from Gannon University and has been a member of the Healthcare Business Women Association since 2002.

We believe that Ms. Connealy's current and prior experience at leading life science companies, including as a chief financial officer, and her financial experience and expertise provide her with the qualifications and skills to serve on our Board.

Eric S. Fain, M.D.

Dr. Fain has served as a member of our Board since January 2023. Prior to that, he served as a director of Legacy Orchestra since November 2018. He previously served as a strategic advisor and a consultant to BackBeat, one of Legacy Orchestra's predecessors and now our wholly-owned subsidiary, from October 2017 to November 2018. Since July 2018, he has served as the President and Chief Executive Officer of Procyrion, Inc., a development stage medical device company developing catheter-based circulatory support technologies for congestive heart failure patients. Previously, he was the Group President of Cardiovascular and Neuromodulation at Abbott Laboratories from January 2017 until July 2017, a multinational medical devices and healthcare company, following its acquisition of medical device company St. Jude Medical, Inc. Dr. Fain became Group President of St. Jude Medical, Inc. in January 2015, where he was responsible for global sales, marketing and clinical affairs across the entire St. Jude Medical portfolio worldwide. Dr. Fain joined St. Jude Medical in 1997 as Vice President of Systems Development as part of the company's acquisition of Ventritex, Inc., where he had worked since 1987. He went on to become Senior Vice President of Clinical/Regulatory Affairs for the St. Jude Medical Cardiac Rhythm Management Division ("CRMD") in 1998. He was later promoted to Executive Vice President, Development and Clinical/Regulatory Affairs for CRMD in 2005 and then President of CRMD in 2007. Prior to his role as Group President, Dr. Fain was President of the company's Implantable Electronic Systems Division beginning in 2012 when its CRMD and Neuromodulation Divisions merged. Dr. Fain earned an M.D. from Stanford University School of Medicine and a Sc.B. degree in applied math/biology from Brown University.

We believe that Dr. Fain's extensive senior management experience in the life sciences sector, including his service as a top executive at one of the market leading global commercial companies in the medical device sector, as well as his medical background and financial and transaction structuring experience provide him with the qualifications and skills to serve on our Board.

Eric A. Rose, M.D.

Dr. Rose has served as a member of our Board since January 2023. Prior to that, he served as a director of Legacy Orchestra since December 2018. He previously served as a strategic advisor to Legacy Orchestra from July 2018 to December 2018. Since February 2022, Dr. Rose has served as Chief Medical Officer of Mesoblast Limited (Nasdaq: MESO), a Nasdaq-listed leader in cellular medicines for inflammatory diseases, where he has served as a director since April 2013. From October 2018 until June 2021, Dr. Rose served as Chairman of the board of directors of SIGA Technologies, Inc. (Nasdaq: SIGA), a Nasdaq-listed developer of antiviral drugs directed at potential agents of bioterror. Previously, he served as SIGA Technologies, Inc.'s Executive Chairman from October 2016 to December 2018, as its Chairman from January 2007 to October 2016 and as its Chief Executive Officer from January 2007 to October 2016. SIGA Technologies, Inc. filed voluntary proceedings under Chapter 11 of the United States Bankruptcy Code in September 2014 and exited from bankruptcy protection in April 2016. In addition to his roles at SIGA Technologies, Inc., Dr. Rose held a position as Executive Vice President for Life Sciences at MacAndrews & Forbes Incorporated, the diversified holding company wholly owned by investor Ronald O. Perelman and a related party to SIGA, from 2007 until December 2016. Dr. Rose chaired the Department of Health Evidence & Policy at the Icahn School of Medicine at Mount Sinai from 2008 to 2013 and has served as a professor in the Department of Population Health Science & Policy since 2008. From 1994 through 2007, he served as Chairman of the Department of Surgery and Surgeon-in-Chief of the Columbia Presbyterian Center of New York Presbyterian Hospital. In 2014, Dr. Rose became a director of ABIOMED, Inc. (Nasdaq: ABMD), a Nasdaq-listed leading provider of medical devices that provide circulatory support, and currently serves on its audit committee. He has been a member of the American Association for Thoracic Surgery since 1986 and a member and former president of the International Society of Heart and Lung Transplantation since 1982. Dr. Rose earned a B.A. from Columbia College and an M.D. from Columbia University College of Physicians and Surgeons.

We believe that Dr. Rose's extensive medical background, including his role in leading a cardiology program at a leading hospital, and his senior management experience in the life sciences sector and medical research and financial experience provide him with the qualifications and skills to serve on our Board.

Geoffrey W. Smith

Mr. Smith has served as a member of our Board since January 2023. Prior to that, he served as a director of Legacy Orchestra since May 2018. He previously served on the boards of Legacy Orchestra's predecessors and now our wholly-owned subsidiaries, Caliber, BackBeat, and FreeHold, from March 2013 to November 2018. He is a co-founder and, since April 2004, has been a General Partner of Ascent Biomedical Ventures, LLC ("ABV"), a New York City-based venture capital firm focused on early-stage life sciences investments and an investor in Caliber, BackBeat and FreeHold. Funds managed by ABV continue to be our stockholders. Mr. Smith has represented ABV on the board of directors of Azevan Pharmaceuticals Inc., a clinical stage, small molecule drug development company developing novel therapeutics to treat stress-related CNS disorders and neurodegenerative conditions, since August 2005 and BlinkBio Inc., a biotechnology company developing tunable drug conjugate therapies for the treatment of cancer, since June 2012. He is also the founder and, since February 2016, has been the Managing Partner of Digitalis Ventures, a venture capital firm that invests across the full continuum of the healthcare ecosystem. He has represented Digitalis as a director of Terray Therapeutics, which is developing a novel spatially encoded screening and optimization platform to develop treatments for historically intractable causes of human disease, since April 2019; Base5 Genomics, which is developing novel sequencing solutions that reveal the full genomic diversity in humans and other organisms, since May 2019; GRO Biosciences, Inc., which is leveraging technologies from computational protein design and synthetic biology to develop best-in-class protein therapeutics, since August 2017; Elemental Machines, which provides a sensor-based platform for the monitoring and assessment of lab and environmental parameters affecting critical scientific and industrial processes, since March 2018; and CareDox Inc., which provides pediatric healthcare and data services, since May 2020. From January 2015 to January 2016, he also served as the Managing Director of Mars Ventures, which was the strategic venture capital arm of Mars, Inc., investing at the intersection of human health, technology and agriculture. Mr. Smith has served as a Trustee of The Jackson Laboratory since November 2017. He has also been a member of the Scientific Advisory Board for Brigham & Women's Hospital in Boston since December 2013. He has also served as the Chair of the Board of Governors for the Bard Early College since December 2013. Previously, he was the founding Director of the Mount Sinai Institute of Technology and a professor in the Department of Population Health Science & Policy at the Icahn School of Medicine at Mount Sinai. Mr. Smith earned a B.A. with honors from Williams College and a J.D. from the University of Pennsylvania Law School.

We believe that Mr. Smith's extensive experience as an investor in life science companies, including his service as a general partner and managing partner of venture capital firms focused on the life sciences sector, and his extensive knowledge of our business provide him with the qualifications and skills to serve on our board of director.

Family Relationships

There are no family relationships among any of the individuals who serve as our directors or executive officers.

Composition of the Our Board

Our business and affairs are managed under the direction of our Board. The Board currently consists of seven members. Mr. Hochman serves as Chairperson of the Board. Mr. Fain serves as the lead independent director. The primary responsibilities of the Board is to provide oversight, strategic guidance, counseling and direction to our management. The Board meets on a regular basis and on an ad hoc basis as required.

In accordance with the terms of the Charter and Bylaws, the Board are divided into three classes with staggered three-year terms, as follows:

- The Class I directors are Eric A. Rose, M.D. and Jason Aryeh, and their term will expire at the annual meeting of stockholders to be held in 2024;

- The Class II directors are Pamela Y. Connealy and Geoffrey W. Smith, and their term will expire at the annual meeting of stockholders to be held in 2025; and

- The Class III directors are David P. Hochman, Darren R. Sherman and Eric S. Fain, M.D., and their term will expire at the annual meeting of stockholders to be held in 2026.

At each annual meeting of stockholders to be held after the initial classification, the successors to directors whose terms will then expire will be elected to serve from the time of election and qualification until the third annual meeting following their election. The authorized number of directors that shall constitute the Board will be determined exclusively by the Board. Any increase or decrease in the number of directors will be apportioned among the three classes so that, as nearly equal as practicable, each class will consist of one-third of the directors. No decrease in the number of directors constituting the Board will shorten the term of any incumbent director. Our directors may be removed, at any time, but only for cause and only by the affirmative vote of at least a majority of the total voting power of the outstanding shares of voting stock then entitled to vote at an election of directors.

Subject to applicable law and the Charter and subject to the rights of the holders of any series of our Preferred Stock, any vacancy on the Board shall be filled only by the Board and not by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

Director Independence

Nasdaq rules generally require that independent directors must comprise a majority of a listed company's board of directors. Based upon information requested from and provided by each proposed director concerning his or her background, employment and affiliations, including family relationships, we have determined that each of Messrs. Rose, Aryeh, Smith and Fain and Ms. Connealy, representing a majority of the directors, are "independent" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements and rules of Nasdaq. Mr. Fain serves as the lead independent director. In making these determinations, the Board considered the current and prior relationships that each non-employee director has with us and all other facts and circumstances the Board deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled "*Certain Relationships and Related Transactions*."

Role of Board in Risk Oversight Process

The Board has extensive involvement in the oversight of risk management related to us and our business as a whole, including its strategy, business performance, capital structure, management selection, compensation programs, stockholder engagement, corporate reputation, environmental, social, and governance matters, and ethical business practices. The Board discharges various aspects of its oversight responsibilities through its standing committees, which in turn report to the Board regularly regarding their activities. The audit committee represent the Board by periodically reviewing our accounting, reporting and financial practices, including the integrity of our financial statements and the surveillance of administrative and financial controls, as well as enterprise risk management, cyber risk and review of related party transactions. Through its regular meetings with management, including the finance, legal, internal audit and information technology functions, the audit committee reviews and discusses all significant areas of our business and summarizes for the Board all areas of risk and the appropriate mitigating factors. The nominating and corporate governance committee provides oversight over compliance with legal and regulatory requirements, ethics and whistleblower matters. The compensation committee reviews the company's incentive compensation arrangements to determine whether they encourage excessive risk-taking and discusses with management the relationship between risk management policies and practices and compensation. In addition, the Board receives periodic detailed operating performance reviews from management.

Committees of the Board

Our Board has an audit committee, compensation committee and nominating and corporate governance committee. Our Board has adopted charters for each of these committees, which comply with the applicable requirements of current SEC and Nasdaq rules. We will comply with future requirements to the extent applicable. Copies of the charters for each committee is available on the investor relations portion of our website. The composition and responsibilities of each of the committees of our Board are as set forth below. Members will serve on these committees until their resignation or removal or until otherwise determined by our Board. Our Board may from time to time establish other committees.

Audit Committee

Our audit committee currently consists of Pamela A. Connealy, Geoffrey W. Smith and Jason Aryeh, with Pamela A. Connealy serving as the chairperson. The composition of our audit committee meets the requirements for independence under the current

Nasdaq listing standards and SEC rules and regulations. Each member of our audit committee is financially literate. Our Board has determines that Ms. Connealy is an “audit committee financial expert” as defined in Item 407(d)(5)(ii) of Regulation S-K. This designation does not impose on either any duties, obligations or liabilities that are greater than are generally imposed on members of our audit committee and the Board. Our audit committee is directly responsible for, among other things:

- selecting a firm to serve as the independent registered public accounting firm to audit our financial statements;
- ensuring the independence of the independent registered public accounting firm;
- discussing the scope and results of the audit with the independent registered public accounting firm and reviewing, with management and that firm, our interim and year-end operating results;
- establishing procedures for employees to anonymously submit concerns about questionable accounting or audit matters;
- considering the adequacy of our internal controls and internal audit function;
- reviewing material related party transactions or those that require disclosure; and
- approving or, as permitted, pre-approving all audit and non-audit services to be performed by our independent registered public accounting firm.

Compensation Committee

Our compensation committee currently consists of Eric Fain, Geoffrey W. Smith and Eric Rose, with Eric Fain serving as the chairperson. Each member of this committee is a non-employee director, as defined by Rule 16b-3 promulgated under the Exchange Act, and an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code, and meets the requirements for independence under the current Nasdaq listing standards. Our compensation committee is responsible for, among other things:

- reviewing and approving, or recommending that our Board approve, the compensation of our executive officers;
- reviewing and recommending to our Board the compensation of our directors;
- administering our stock and equity incentive plans;
- reviewing and approving, or making recommendations to our Board with respect to, incentive compensation and equity plans; and
- reviewing our overall compensation philosophy.

Nominating and Corporate Governance Committee

Our nominating and governance committee currently consists of Jason Aryeh, Eric Fain and Eric Rose, with Jason Aryeh serving as the chairperson. Each of Jason Aryeh, Eric Fain and Eric Rose meets the requirements for independence under the current Nasdaq listing standards. Our nominating and governance committee is responsible for, among other things:

- identifying and recommending candidates for membership on our Board;
- reviewing and recommending our corporate governance guidelines and policies;
- reviewing proposed waivers of the code of conduct for directors and executive officers;
- overseeing the process of evaluating the performance of our Board; and

- assisting our Board on corporate governance matters.

Code of Ethics

We adopted a code of ethics that applies to all of our employees, officers and directors, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. The full text of our code of ethics is available on the investor relations section of our website. We will disclose future amendments to our code of business conduct and ethics, or any waivers of such code, on our website.

Compensation Committee Interlocks and Insider Participation

No member of the compensation committee was at any time during fiscal year 2022, or at any other time, one of our officers or employees. None of our executive officers has served as a director or member of a compensation committee (or other committee serving an equivalent function) of any entity, one of whose executive officers served as a director of our Board or member of our compensation committee.

Limitation of Liability and Indemnification of Directors and Officers

Our Charter and Bylaws limit a director's and officer's liability to the fullest extent permitted under the DGCL. The DGCL provides that directors and officers of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors or officers, except for liability:

- for any transaction from which the director or officer derives an improper personal benefit;
- for any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- for a director under Section 174 of the DGCL;
- for any breach of a duty of loyalty to the corporation or its stockholders; or
- for an officer in any action by or in the right of the corporation.

If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors or officers, then the liability of the directors and officers will be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Delaware law and our Bylaws provide that we will, in certain situations, indemnify our directors and officers and may indemnify other employees and other agents, to the fullest extent permitted by law. Any indemnified person is also entitled, subject to certain limitations, to advancement, direct payment, or reimbursement of reasonable expenses (including attorneys' fees and disbursements) in advance of the final disposition of the proceeding.

In addition, we entered into separate indemnification agreements with each of our directors and officers. These agreements, among other things, require us to indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of their services as one of our directors or officers or any other company or enterprise to which the person provides services at our request.

We maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers. We believe these provisions in our Charter and Bylaws and these indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers, or control persons, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

EXECUTIVE AND DIRECTOR COMPENSATION

HSAC2 Executive Officers and Director Compensation Prior to Completion of the Business Combination

Prior to the closing of the Business Combination, none of HSAC2's executive officers or directors received any cash compensation for services rendered to HSAC2.

Legacy Orchestra and Current Executive Compensation

This section discusses the material components of the executive compensation program for Legacy Orchestra's executive officers who would have been the "named executive officers" if Legacy Orchestra was subject to the reporting requirements under the Exchange Act. For the fiscal year ending December 31, 2022, Legacy Orchestra's "named executive officers" and their positions were as follows:

- David P. Hochman, Chief Executive Officer and Chairman of the Orchestra Board
- Darren R. Sherman, President, Chief Operating Officer and a Director of Orchestra
- Michael D. Kaswan, Former Chief Financial Officer

Unless the context otherwise requires, all references in this section to the "Company," "Orchestra," or "it" refer to the business of Legacy Orchestra and its subsidiaries prior to the consummation of the Business Combination and to the Company and its subsidiaries after the Business Combination. Unless the context otherwise requires, references in this section to "common stock" refer to Legacy Orchestra Common Stock. All share counts in this section are shown on a post-Business Combination basis.

We are an emerging growth company and a smaller reporting company. Therefore, we are be subject to reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder non-binding advisory approval of any golden parachute payments not previously approved.

Summary Compensation Table

The following table presents summary information regarding the total compensation that was awarded to, earned by or paid to Orchestra's named executive officers for the years ended December 31, 2022 and December 31, 2021.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($)(1)(2)	Option Awards ($)(1)(2)	Non-Equity Incentive Plan Compensation ($)(3)	Total ($)
David P. Hochman	2022	395,000	—	63,000	2,303,394	395,000	3,156,394
Chief Executive Officer & Chairman	2021	395,000	—	38,709	—	276,500	710,209
Darren R. Sherman	2022	395,000	—		2,334,615	395,000	3,124,615
President & Chief Operating Officer	2021	395,000	—	19,355	—	276,500	690,855
Michael D. Kaswan	2022	375,000	50,000(4)	459,830	843,663	183,293	1,911,786
Former Chief Financial Officer	2021	—	—	—	—	—	—

(1) The amounts shown in this column represent the aggregate grant date fair value of stock awards and option awards granted to Orchestra's named executive officers computed in accordance with FASB ASC 718. Such grant-date fair value does not take into account any estimated forfeitures related to service-vesting conditions. See Note 9 to Orchestra's consolidated financial statements for the fiscal years ended December 31, 2022 and 2021 included elsewhere in this prospectus for a description of Orchestra's assumptions used in the calculation.

(2) See "— *Narrative Disclosure to Summary Compensation Table — Equity-Based Incentive Awards*."

(3) See "— *Narrative Disclosure to Summary Compensation Table — Non-Equity Incentive Compensation*."

(4) Represents the Funding Bonus paid to Mr. Kaswan. See "— *Narrative Disclosure to Summary Compensation Table — Certain Provisions in Michael D. Kaswan's Employment Agreement.*"

Narrative Disclosure to Summary Compensation Table

Overview

The primary elements of compensation for Orchestra's named executive officers are base salary, annual performance bonuses and equity awards. Orchestra's named executive officers also participate in employee benefit plans and programs that Orchestra offers to its other employees, as described below. Orchestra's executive compensation program is designed to attract, retain and reward key employees, to incentivize them based on the achievement of key performance goals, and to align their interests with the interests of Orchestra stockholders.

Annual Base Salary

The salaries of Orchestra's named executive officers are specified in their respective employment agreements, which, with respect to Messrs. Hochman and Sherman were negotiated with Orchestra's executive officers in connection with the formation of the business through mergers that were completed on May 31, 2018 with each of (i) Caliber Therapeutics, Inc., (ii) BackBeat Medical, Inc. and (iii) FreeHold Surgical, Inc. Mr. Kaswan's salary was negotiated in connection with his hiring in January 2022.

Non-Equity Incentive Compensation

Orchestra's named executive officers are entitled to receive non-equity incentive plan bonuses pursuant to the terms of their respective employment agreements. Under the terms of these employment agreements, the amounts of these bonuses and the performance metrics and goals required to receive those bonus amounts are determined by the Orchestra Board based on appropriate comparative benchmarks.

For 2022, annual non-equity incentive plan bonuses for Orchestra's named executive officers were based on progress made (i) relating financing and matters relating to potentially becoming a public company (ii) by the focal therapies group with respect to certain clinical, regulatory and other matters; (ii) by the bioelectronic therapies group with respect to entering into the Medtronic Agreement, clinical studies, product development, as well as clinical and regulatory development; and (iii)

For 2022, the target bonus for each of Messrs. Hochman and Sherman was 100% of their respective base salaries, and the target bonus for Mr. Kaswan was 50% of his base salary. Based on Orchestra's progress against the performance goals set by its compensation committee, the compensation committee determined to pay each of its named executive officers 100% of their target bonuses for 2022. The actual annual non-equity incentive plan cash bonuses awarded to each named executive officer for 2022 performance are set forth above in the Summary Compensation Table in the column titled "Non-Equity Incentive Plan Compensation."

For 2021, annual bonuses for Orchestra's named executive officers were based on progress made (i) by the Focal Therapies group with respect to certain clinical, regulatory and other matters; (ii) by the bioelectronic therapies group with respect to partnering, clinical studies, product development, clinical and regulatory development and research; and (iii) relating to (a) financing and potentially becoming a public company, (b) auditing matters and reporting matters and (c) strategy, marketing and business development.

For 2021, the target bonus for each of Messrs. Hochman and Sherman was 100% of their respective base salaries. Based on Orchestra's progress against the performance goals set by its compensation committee, the compensation committee determined to pay each of its named executive officers 70% of their target bonuses for 2021. The actual annual cash bonuses awarded to each named executive officer for 2021 performance are set forth above in the Summary Compensation Table in the column titled "*Non-Equity Incentive Plan Compensation.*"

Equity-Based Incentive Awards

Orchestra's equity-based incentive awards are designed to align its interests and the interests of its stockholders with those of its employees and consultants, including the named executive officers. The Orchestra Board is responsible for approving equity grants based on recommendations of the compensation committee. As described below, each of the named executive officers is entitled to certain equity awards pursuant to the terms of his employment agreement.

In June 2021, Legacy Orchestra's board of directors granted 14,742 restricted stock units to Mr. Hochman and 7,371 restricted stock units to Mr. Sherman. These equity awards were granted as part of the named executive officers' bonuses for 2020, a portion of which the named executive officers agreed would be paid in equity to help preserve Legacy Orchestra's cash. One hundred percent of the restricted stock units granted pursuant to these awards vested on the date of grant.

All equity awards disclosed in the Summary Compensation Table were made under the 2018 Plan.

Employment Agreements with Orchestra's Named Executive Officers

Each of Orchestra's named executive officers is party to an employment agreement with Orchestra's that sets forth the terms and conditions of their employment. Each such agreement provides for "at will" employment. The material terms of the employment agreements with the named executive officers are described below.

Certain Provisions in David P. Hochman's Employment Agreement in Existence Prior to January 26, 2023

On May 31, 2018, Orchestra entered into an employment agreement with Mr. Hochman that governed the terms of his employment with Orchestra as its Chief Executive Officer (the "Prior Hochman Agreement") until his employment agreement was amended on January 26, 2023. Pursuant to the Prior Hochman Agreement, Mr. Hochman received an annual base salary of $395,000. In addition to this base compensation, Mr. Hochman was eligible to receive a discretionary annual bonus during each fiscal year of his employment, such amount, and the performance metrics and goals required to receive such amount, to be determined by the Orchestra Board based on appropriate comparative benchmarks. The Prior Hochman Agreement also provided that he receive common stock or options to acquire common stock (at his election) in the amount of four percent of the fully-diluted shares of Orchestra Common Stock as of the date of the final closing of the private placement of Orchestra's Series B Preferred Stock (the "Hochman Series B Grant"). In accordance with the Hochman Series B Grant, Mr. Hochman was (i) granted options to purchase 263,821 shares of common stock at an exercise price of $4.30 per share on August 7, 2018 and (ii) 46,500 shares of restricted stock on August 7, 2019, which shares were issued late due to an administrative omission (the Orchestra Board determined to vest all of these shares immediately in light of the delay in their issuance). The final closing of Orchestra's private placement of Series B Preferred Stock did not take place until October 18, 2018, and Mr. Hochman was granted 55,345 shares of restricted stock in August 2019 pursuant to the Hochman Series B Grant.

In addition, the Prior Hochman Agreement provided that Mr. Hochman was to receive common stock or options to acquire common stock (at his election), in an amount such that, together with the options and restricted stock issued pursuant to the Hochman Series B Grant, he would receive common stock or options to acquire common stock in an amount equal to four percent of the fully-diluted shares of common stock as of the earlier of (A) the date of the final closing of a Follow-On Offering (as such term is defined in the Investors' Rights Agreement, dated May 31, 2018, by and among Orchestra and investors signatory thereto, as amended (the "Investors' Rights Agreement")) and (B) the effective date of Orchestra's first firm commitment public offering of its common stock under the Securities Act (such earlier date, the "Follow-On Offering Date"). Orchestra's private placement of Series B-1 Preferred Stock would have qualified as a Follow-On Offering; however, pursuant to the terms of the Investors' Rights Agreement, the Orchestra Board and Orchestra's stockholders waived the treatment of the Series B-1 Preferred Stock offering as a Follow-On Offering. The Series D Financing qualified as a Follow-On Offering, and, accordingly, Mr. Hochman was entitled to receive 677,890 shares of common stock or options to acquire common stock. Of this amount, Mr. Hochman received 15,500 shares of restricted stock and 546,140 options to acquire common stock in 2022 and 116,250 options to acquire common stock in 2023.

Certain Provisions in Darren R. Sherman's Employment Agreement in Existence Prior to January 26, 2023

On May 31, 2018, Orchestra entered into an employment agreement with Mr. Sherman that governed the terms of his employment with Orchestra as its President and Chief Operating Officer (the "Prior Sherman Agreement" and, together with the Prior Hochman Agreement, the "Prior Executive Agreements") until his employment agreement was amended on January 26, 2023. Pursuant to the Prior Sherman Agreement, Mr. Sherman received an annual base salary of $395,000. In addition to this base compensation, Mr. Sherman was eligible to receive a discretionary annual bonus during each fiscal year of his employment, such amount, and performance metrics and goals required to receive such amount, to be determined by the Orchestra Board based on appropriate comparative benchmarks. The Prior Sherman Agreement also provided that he receive common stock or options to acquire common stock (at his election) in the amount of four percent of the fully-diluted shares of common stock as of the date of the final closing of the private placement of Orchestra's Series B Preferred Stock (the "Sherman Series B Grant"). In accordance with the Sherman Series B Grant, Mr. Sherman was granted options to purchase 310,321 shares of common stock at an exercise price of $4.30 per share on August 7, 2018. The final

closing of Orchestra's private placement of Series B Preferred Stock did not take place until October 18, 2018, and Mr. Sherman was granted 55,345 shares of restricted stock in August 2019 pursuant to the Sherman Series B Grant.

In addition, the Prior Sherman Agreement provided that he was to receive common stock or options to acquire common stock (at his election), in an amount such that, together with the options and restricted stock issued pursuant to the Sherman Series B Grant, he would have received common stock or options to acquire common stock in an amount equal to four percent of the fully-diluted shares of Orchestra Common Stock as of the Follow-On Offering Date. Orchestra's private placement of Series B-1 Preferred Stock would have qualified as a Follow-On Offering; however, pursuant to the terms of the Investors' Rights Agreement, the Orchestra Board and Orchestra's stockholders waived the treatment of the Series B-1 Preferred Stock offering as a Follow-On Offering. The Series D Financing qualified as a Follow-On Offering, and, accordingly, Mr. Sherman was entitled to receive 677,890 shares of common stock or options to acquire common stock. Of this amount, Mr. Sherman received 561,640 options to acquire common stock in 2022 and 116,250 options to acquire common stock in 2023.

Provisions Applicable to Option Awards Made Under the Prior Executive Agreements

Any option grant made under the Prior Executive Agreements has the following terms:

- upon a Change of Control (as defined in the Prior Executive Agreements) of Orchestra, any unvested options will become fully vested; and
- if the executive is terminated without Cause (as defined in the Prior Executive Agreements), or voluntarily terminates his employment with Good Reason (as defined in the Prior Executive Agreements), any unvested options will become fully vested.

All options and restricted stock granted pursuant to Prior Executive Employment Agreements vested as follows: 33% of any options or restricted stock awarded were fully vested at the time of the award and 67% vested on a quarterly basis over three years, with the first vesting date being the end of the first calendar quarter after the date of the award.

Certain Provisions in the Amended Employment Agreements of David P. Hochman and Darren R. Sherman Entered into on January 26, 2023

On January 26, 2023 (the "Amended Employment Agreement Date"), Orchestra entered into employment agreements with each of Mr. Hochman and Mr. Sherman that governs the terms of their employment with Orchestra. The agreements provide that Mr. Hochman shall serve as Chief Executive Officer and Orchestra BioMed Founder and Mr. Sherman shall serve as President, Chief Operating Officer, and Orchestra BioMed Founder. Employment under the agreements is "at will" although Mr. Hochman and Mr. Sherman may be entitled to severance upon certain terminations as described below. Pursuant to the agreements, the executives receive annual base salary ($595,000 for Mr. Hochman and $495,000 for Mr. Sherman). In addition to this base compensation, the executives are each eligible to receive a discretionary annual bonus during each fiscal year of his employment with a target amount of 80% of base salary, with the performance metrics and goals required to receive such amount to be determined by the Orchestra Board in consultation with Orchestra's Chief Executive Officer.

The agreements also provide for a future grant of equity compensation (the "Equity Grant") to each of the executives, to be made as soon as reasonably practicable following the beginning of Orchestra's first open trading window, so that the executive's long-term equity holdings in Orchestra are at least 4.6% of Common Stock in the case of Mr. Hochman and 4.3% in the case of Mr. Sherman. These percentages assume the future grant is in the form of options with a four-year vesting schedule commencing as of the Closing Date. However, the agreements contemplate that if instead the award is restricted stock units, the number of covered shares of Common Stock will be reduced by a ratio based on two shares covered by restricted stock units being equal to three shares covered by stock options and that the award will vest over a to-be-agreed vesting schedule over a minimum of three years. Pursuant to the Equity Grant, on July 20, 2023, (i) Mr. Hochman was granted options to purchase 232,500 shares of common stock at an exercise price of $7.42 per share and 465,000 restricted stock units ("RSUs") and (ii) Mr. Sherman was granted 539,667 RSUs.

Board Membership Provisions

The employment agreements provide that so long as each of Messrs. Hochman and Sherman remain in their current positions (Chief Executive Officer for Mr. Hochman and President and Chief Operating Officer for Mr. Sherman), Orchestra shall nominate

each of them to serve as a member of the Orchestra Board. Messrs. Hochman and Sherman's service as a member of the Orchestra Board shall end upon certain specified events, including the termination of their employment and the expiration of their then current term if not reelected by Orchestra's stockholders.

Termination and Severance Provisions

With respect to the each of Messrs. Hochman and Sherman, if Orchestra terminates his employment without Cause (as defined below), if he voluntarily resigns with Good Reason (as defined below), or in the event of his death, and subject to an effective release of claims, Orchestra will pay or provide him or his estate with continued base salary plus target bonus for 12 months (the "Severance Obligations"). In addition, in the event of a termination without Cause or resignation for Good Reason, and subject to an effective of release of claims, Orchestra will pay or provide the executive with (i) if he validly elects to continue his healthcare coverage under applicable law, reimbursement of the applicable premium for up to 12 months, (ii) an extended stock option post-termination exercise period of up to 12 months, and (iii) all equity awards held by the executive granted prior to the Closing Date will vest to the same extent such awards would have vested had the executive provided an additional 12 months of services. If the termination without Cause or resignation for Good Reason occurs within the period beginning three months prior to a Change of Control (as defined in the 2023 Plan) and ending 12 months following a Change of Control, then, subject to an effective release of claims, the continued Severance Obligations shall be increased to 150% of annual base salary and target bonus, and (ii) all unvested equity awards held by the executive shall vest in full.

In addition, upon any termination of employment, each of Messrs. Hochman and Sherman shall be entitled to payment of accrued, but unpaid, base salary and reimbursement of previously and properly incurred business expenses.

Other Change of Control Provisions Not Part of Severance

The employment agreements provide that if a Change of Control occurs and the acquirer or surviving corporation refuses to assume or substitute for the executive's outstanding equity awards, the equity awards shall vest in full as of the date immediately preceding the Change of Control.

Definition of Cause

"Cause" means each of:

- executive's breach of any of his obligations under the restrictive covenants section of his employment agreement;
- executive's breach of any of his obligations under his employment agreement (other than the restrictive covenants section of his agreement), which, to the extent curable, has not been cured within 30 days after the executive has been provided written notice of such breach;
- executive being convicted of, or pleading guilty or nolo contendere to, or being indicted for, any felony or any misdemeanor involving theft, fraud, dishonesty or moral turpitude; or
- fraud or embezzlement against Orchestra.

Definition of Good Reason

"Good Reason" means each of:

- any change in the executive's position, title or reporting relationship with Orchestra that diminishes in any material respect the executive's authority, duties, or responsibilities; provided, however, that a change in authority, duties, or responsibilities due to Orchestra becoming a division, subsidiary, or other similar part of a larger organization shall not by itself constitute Good Reason;
- any material reduction in the executive's base compensation;

- the relocation of the executive's principal office or principal place of employment by more than fifty miles; or
- a material breach of the employment agreement by Orchestra;

provided, however, that the executive must provide written notice within 60 days of the occurrence of the potential Good Reason trigger; if curable, Orchestra must fail to cure the potential Good Reason trigger within 60 days of receipt of notice, and the executive must resign within 60 days following the expiration of the 60-day cure period.

Golden Parachute Provisions

The employment agreements contain customary golden parachute provisions providing that if, in connection with a Change of Control, amounts would constitute "parachute payments" under Section 280G of the Internal Revenue Code, and be subject to an excise tax under Section 4999 of the Internal Revenue Code, amounts will either be (i) reduced, or (ii) paid in full, whichever results in the greater after tax amount to the executive.

Certain Provisions in Michael D. Kaswan's Employment Agreement

On January 9, 2021, Orchestra entered into an employment letter agreement with Mr. Kaswan (the "Kaswan Agreement"). Pursuant to the terms of the Kaswan Agreement, Mr. Kaswan served as Orchestra's Chief Financial Officer and was entitled to an annual base salary of $375,000. In addition, pursuant to the Kaswan Agreement, Mr. Kaswan:

- was entitled to an annual incentive based bonus with a target of 50% of his base salary starting with the 2022 calendar year (the "Annual Bonus"), which was to be awarded based on the achievement of milestones determined by the Company's Board of Directors.
- was entitled to a one-time bonus payment in the amount of $50,000 (the "Funding Bonus") within 15 business days following the closing (the "Series D Closing") of the Company's planned Series D Financing of at least $100 million in gross proceeds (the "Funding Bonus"), which was paid in July 2022;
- was entitled to a one-time bonus payment of $50,000 (the "Anniversary Bonus") within fifteen (15) business days following the date which was 18 months from his employment start date ("One Year Anniversary"), which was paid in June 2023 in connection with Mr. Kaswan's departure from the Company on June 5, 2023.
- received an initial grant of 116,907 shares of restricted stock pursuant to the 2018 Plan, one third of which vested 12 months from Mr. Kaswan's starting date with Orchestra, with the remainder vesting in equal quarterly installments over a two-year period from the date that was 12 months from Mr. Kaswan's starting date with Orchestra; and
- received additional ten-year options to acquire common stock of the Company representing 1.25% of the fully diluted common shares outstanding as of the closing of the Series D Financing (the "Additional Grant"), vesting in equal quarterly installments over a three-year period from the date of grant.

Notwithstanding the terms of Kaswan Agreement, in lieu of providing Mr. Kaswan with the Additional Grant, the Board approved and, Mr. Kaswan agreed to receive a grant of 16,638 shares of restricted stock in April 2022 and an option to purchase 192,566 shares of common stock with an exercise price $10.00 per share in August 2022.

Termination and Severance Provisions

Pursuant to the Kaswan Agreement, upon any termination of Mr. Kaswan's employment with the Company, he is entitled to the following: (i) any earned but unpaid base salary; (ii) reimbursement for reimbursable expenses incurred by Mr. Kaswan prior to the date of termination in accordance with the Kaswan Agreement; (iii) vested and accrued benefits, if any, to which Mr. Kaswan may have been be entitled under the Kaswan Agreement or under the Company's employee benefit plans as of the date of termination; and (iv) any additional amounts or benefits due under any applicable plan, program, agreement or arrangement of the Company, including the 2018

Plan, subject to the terms of such plan, program, agreement or arrangement (the amounts and benefits described in clauses (i) through (iv) above, collectively, the "Kaswan Accrued Benefits").

If Mr. Kaswan's employment was terminated without Cause or for Good Reason (each as defined in the Kaswan Agreement), then, in addition to the Accrued Benefits: (a) conditioned on, among other things, Mr. Kaswan's execution in favor of the Company (including its subsidiaries and affiliates and its and their officers, directors and employees) of a general release of all claims (the "Release") becoming irrevocably effective, the Company is required to (i) continue to pay to Mr. Kaswan, as severance, his base salary for six months (subject to extension as provided below, the "Severance Period") subject to deductions and withholdings (the "Severance Payments"), (ii) pay Mr. Kaswan the Anniversary Bonus if such termination occurs after the initial 12 months of the commencement of Mr. Kaswan's employment with the Company and any earned but unpaid Annual Bonus for the year prior to such termination, each within 10 days after such termination, (iii) pay Mr. Kaswan the Funding Bonus if earned but unpaid on or prior to such termination, or if the Series D Closing occurs following such termination but prior to the end of the Severance Period, and (iv) reimburse Mr. Kaswan for the premiums he pays to continue medical benefits for Mr. Kaswan and his eligible dependents under applicable law (COBRA) for the Severance Period or, if earlier, until Mr. Kaswan becomes eligible for benefits for a subsequent employer, (b) Mr. Kaswan is to vest in the unvested options or shares that were scheduled to vest during the Severance Period (subject to acceleration as provided below), and (c) Mr. Kaswan is able to exercise vested options during the Severance Period. If such a termination occurred within the period beginning 3 months prior to a Change of Control (as defined in the Kaswan Agreement) and ending 12 months following a Change of Control (the "Change of Control Period"), and conditioned upon his execution of the Release, there will be full acceleration of equity vesting. The Severance Period shall be nine months if Mr. Kaswan's termination occurred on or after the One Year Anniversary and 12 months if his termination occurred during the Change of Control Period.

Consulting Agreement Entered into with Mr. Kaswan in Connection with his Departure

On June 5, 2023, Orchestra and Mr. Michael Kaswan mutually agreed to terms pursuant to which Mr. Kaswan would step down as the Company's Chief Financial Officer and separate from employment with the Company effective as of June 6, 2023 (the "Separation Effective Date").

In connection with Mr. Kaswan's departure, the Company and Mr. Kaswan entered into a consulting agreement dated as of June 5, 2023 (the "Consulting Agreement"), pursuant to which Mr. Kaswan will provide services to assist the Company in transitioning his prior duties as Chief Financial Officer to Andrew Taylor, the new Chief Financial Officer. In exchange for such services, the Company will pay Mr. Kaswan $36,180 per month for up to six months after the Separation Effective Date. Subject to (a) the Consulting Agreement not being terminated by the Company due to Mr. Kaswan's breach and (b) Mr. Kaswan's execution and non-revocation of a standard general release of all claims, the Company will (i) pay Mr. Kaswan an additional termination payment of $108,540 and (ii) provide that Mr. Kaswan shall be deemed to have another three months' service (or until March 5, 2024) for purposes of vesting of outstanding equity compensation.

Restrictive Covenant Obligations Applicable to All Named Executive Officer Employment Agreements

Pursuant to their employment agreements, each of Orchestra's named executive officers is subject to a one-year post-termination non-solicitation of employees covenant, in addition to his obligations, including a perpetual non-disparagement covenant, under his confidential information and intellectual property assignment agreement.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information regarding outstanding stock options and stock awards held by Orchestra's named executive officers as of December 31, 2022. Each of the outstanding equity awards was granted pursuant to the 2018 Plan.

		Option Awards				Stock Awards	
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($/share)	Option Expiration Date	Number of Shares or Units that Have Not Vested (#)[2]	Market Value of Shares or Units of Stock that have not Vested($)[2]
David P. Hochman	8/7/2018	263,821[1]	—	4.30	8/7/2028	—	—
	4/12/2022	8,164[1]	29,579	4.06	4/12/2032	—	—
	8/18/2022	196,157[1]	312,240	10.00	8/18/2032	—	—
Darren R. Sherman	8/7/2018	310,321[1]	—	4.30	8/7/2028	—	—
	4/12/2022	23,664[1]	29,579	4.06	4/12/2032	—	—
	8/18/2022	196,157[1]	312,240	10.00	8/18/2032	—	—
Michael D. Kaswan[3]	2/3/2022	—	—	—	—	116,907[4]	$ 1,073,206
	4/12/2022	—	—	—	—	16,638[4]	$ 152,737
	8/18/2022	32,094[5]	160,472	10.00	8/15/2032	—	—

(1) Options and restricted stock granted to Messrs. Hochman and Sherman vest as follows: 33% of any options or restricted stock awarded will be fully vested at the time of the award and 67% will vest on a quarterly basis over three years, with the first vesting date being the end of the first calendar quarter after the date of the award.

(2) The market value of these shares is based on the estimated value of the common stock on December 31, 2022, which was $9.18 per share.

(3) In accordance with the Consulting Agreement, as of March 5, 2024, Mr. Kaswan's equity awards will no longer vest.

(4) One third of this award vested 12 months from Mr. Kaswan's starting date with Orchestra, with the remainder vesting in equal quarterly installments over a two-year period from the date that was 12 months from Mr. Kaswan's starting date with Orchestra.

(5) These awards vest in equal quarterly installments over a three-year period from the date of grant.

Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan

On December 12, 2022, our Board adopted, subject to the approval by our stockholders, the 2023 Plan. On January 24, 2023, our stockholders approved the 2023 Plan. The 2023 Plan then became effective on January 26, 2023, the date that the closing of the Business Combination occurred.

The following is a summary of the material terms of the 2023 Plan.

Purpose of the 2023 Plan

The purpose of the 2023 Plan is to secure and retain the services of employees, directors and consultants, to provide incentives for such persons to exert maximum efforts for our success and to provide a means by which such persons may be given an opportunity to benefit from increases in value of the Common Stock through the granting of awards under the 2023 Plan. We believe that the awards to be issued under the 2023 Plan will motivate award recipients to offer their maximum effort to Orchestra and help focus them on the creation of long-term value consistent with the interests of Orchestra stockholders. We believe that grants of incentive awards are necessary to enable Orchestra to attract and retain top talent.

Awards

The 2023 Plan provides for the grant of incentive stock options ("ISOs") within the meaning of Section 422 of the Internal Revenue Code, to Orchestra employees and our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock

options (“NSOs”), stock appreciation rights, restricted stock awards, restricted stock unit awards, and other forms of awards to our employees, directors and consultants and any of our affiliates’ employees and consultants.

Authorized Shares

Initially, the maximum number of shares of the Common Stock that could be issued under the 2023 Plan was (i) 3,455,303 shares of Common Stock, plus (ii) an additional number of shares of Common Stock equal to the number of shares subject to outstanding award grants under the 2018 Plan, that, following the effective date of the 2023 Plan, (a) are not issued because the award or any portion of the award expires or otherwise terminates without all of the shares covered by the award having been issued, (b) are not issued because the award or any portion thereof is settled in cash, (c) are forfeited back to or repurchased by us because of the failure to meet a contingency or condition required for the vesting of such shares, (d) are withheld or reacquired to satisfy the exercise, strike or purchase price or (e) are withheld or reacquired to satisfy a tax withholding obligation. In addition, the number of shares of Common Stock that will be reserved for issuance under the 2023 Plan will automatically increase on January 1 of each year for a period of ten years, beginning on January 1, 2024 and ending on (and including) January 1, 2032, in an amount equal to the lesser of (1) 4.8% of the total number of shares of our Common Stock outstanding on December 31 of the immediately preceding year, (2) 3,036,722 shares of Common Stock, and (3) such number of shares of Common Stock determined by our Board or the compensation committee of our Board prior to January 1 of a given year. Notwithstanding anything to the contrary in the foregoing sentence, the aggregate maximum number of shares of Common Stock that may be issued on the exercise of ISOs under the 2023 Plan is 3,455,303 shares, which amount will be increased commencing on January 1, 2023 and ending on (and including) January 1, 2032, in an amount equal to the lesser of (i) 4.8% of the total number of shares of Common Stock outstanding on December 31 of the preceding year, (ii) 3,036,722 shares of Common Stock, and (iii) such number of shares of Common Stock determined by our Board or the Compensation Committee prior to January 1 of a given year. All of the foregoing share numbers are subject to adjustment as necessary to implement any changes in our capital structure (as described below).

Shares of Common Stock subject to awards that will be granted under the 2023 Plan that expire or terminate without being exercised in full will not reduce the number of shares of Common Stock available for issuance under the 2023 Plan. The settlement of any portion of an award in cash will not reduce the number of shares of Common Stock available for issuance under the 2023 Plan. Shares of Common Stock withheld under an award to satisfy the exercise, strike or purchase price of an award or to satisfy a tax withholding obligation will not reduce the number of shares of Common Stock that will be available for issuance under the 2023 Plan. With respect to a stock appreciation right, only shares of Common Stock that are issued upon settlement of the stock appreciation right will count towards reducing the number of shares of Common Stock available for issuance under the 2023 Plan. If any shares of Common Stock issued pursuant to an award are forfeited back to or repurchased or reacquired by us (i) because of a failure to meet a contingency or condition required for the vesting of such shares; (ii) to satisfy the exercise, strike or purchase price of an award; or (iii) to satisfy a tax withholding obligation in connection with an award, the shares of Common Stock that are forfeited or repurchased or reacquired will revert to and again become available for issuance under the 2023 Plan.

Plan Administration

Our Board, or a duly authorized committee of our Board, will administer the 2023 Plan. Our Board, or a duly authorized committee of our Board, may, in accordance with the terms of the 2023 Plan, delegate to one or more of our officers the authority to (i) designate employees (other than officers) to be recipients of specified awards, and to the extent permitted by applicable law, the terms of such awards; and (ii) determine the number of shares of Common Stock to be subject to such awards granted to such employees. Under the 2023 Plan, our Board, or a duly authorized committee of our Board, will have the authority to determine: award recipients; how and when each award will be granted; the types of awards to be granted; the provisions of each award, including the period of exercisability and the vesting conditions applicable to an award; the number of shares of Common Stock or cash equivalent subject to each award; and the fair market value applicable to an award.

Under the 2023 Plan, (i) our Board will not, without stockholder approval, (a) reduce the exercise or strike price of an option or stock appreciation right (other than in connection with a capitalization adjustment), and (b) at any time when the exercise or strike price of an option or stock appreciation right is above the fair market value of a share of Common Stock, cancel and re-grant or exchange such option or stock appreciation right for a new award with a lower (or no) purchase price or for cash, and (ii) a participant’s rights under any award will not be materially adversely impaired by any amendment without the participant’s written consent.

We have also designated a plan administrator to administer the day-to-day operations of the 2023 Plan.

Stock Options

Options will be granted under stock option agreements adopted by our Board. Each option will be designated in writing as an ISO or an NSO. Our Board will determine the exercise price for stock options, within the terms and conditions of the 2023 Plan, except the exercise price of a stock option generally will not be less than 100% (or 110% in the case of ISOs granted to a person who owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our parent or subsidiary corporations (each, a "ten percent stockholder") of the fair market value of Common Stock on the date of grant. Options granted under the 2023 Plan will vest at the rate specified in the stock option agreement as will be determined by our Board. The terms and conditions of separate options need not be identical.

No option will be exercisable after the expiration of ten years (or five years in the case of ISOs granted to a ten percent stockholder) or a shorter period specified in the applicable award agreement. Unless the terms of an optionholder's stock option agreement, or other written agreement between us and the recipient, provide otherwise, if an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death or cause, the optionholder may generally exercise any vested options for a period of three months following the cessation of service. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 18 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service. In the event of a termination for cause, options generally terminate upon the termination date. An optionholder may not exercise an option at any time that the issuance of shares upon such exercise would violate applicable law. Unless provided otherwise in the optionholder's stock option agreement or other written agreement between an optionholder and us, if an optionholder's service relationship with us or any of our affiliates ceases for any reason other than for cause and, at any time during the last thirty days of the applicable post-termination exercise period: (i) the exercise of the optionholder's option would be prohibited solely because the issuance of shares of Common Stock upon such exercise would violate applicable law, or (ii) the immediate sale of any shares of Common Stock issued upon such exercise would violate our trading policy, then the applicable post-termination exercise period will be extended to the last day of the calendar month that begins after the date the award would otherwise expire, with an additional extension of the exercise period to the last day of the next calendar month to apply if any of the foregoing restrictions apply at any time during such extended exercise period. There is no limitation as to the maximum permitted number of extensions. However, in no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of Common Stock issued upon the exercise of a stock option will be determined by our Board and may include (i) cash or check, bank draft or money order payable to us; (ii) a broker-assisted cashless exercise; (iii) subject to certain conditions, the tender of shares of our Common Stock previously owned by the optionholder; (iv) a net exercise of the option if it is an NSO; or (v) other legal consideration acceptable to our Board.

Unless our Board provides otherwise, options or stock appreciation rights generally will not be transferable except by will or the laws of descent and distribution. Subject to approval of our Board or a duly authorized officer, an option may be transferred pursuant to a domestic relations order.

Limitations on ISOs

The aggregate fair market value, determined at the time of grant, of Common Stock with respect to ISOs that are exercisable for the first time by an optionholder during any calendar year under all of our stock plans or plans of our affiliates may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our parent or subsidiary corporations unless (i) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant; and (ii) the term of the ISO does not exceed five years from the date of grant.

Restricted Stock Unit Awards

Subject to the terms of the 2023 Plan, each restricted stock unit award will have such terms and conditions as determined by our Board. A restricted stock unit award represents a participant's right to be issued on a future date the number of shares of Common

Stock that is equal to the number of restricted stock units subject to the award. A participant will not have voting or any other rights as a stockholder of ours with respect to any restricted stock unit award (unless and until shares are actually issued in settlement of a vested restricted stock unit award). A restricted stock unit award will be granted in consideration for a participant's services to us or an affiliate, such that the participant will not be required to make any payment to us (other than such services) with respect to the grant or vesting of the restricted stock unit award, or the issuance of any shares of Common Stock pursuant to the restricted stock unit award. our Board may determine that restricted stock unit awards may be granted in consideration for any form of legal consideration that may be acceptable to our Board and permissible under applicable law. A restricted stock unit award may be settled by cash, delivery of stock (or any combination of Common Stock and cash), or in any other form of consideration determined by our Board and set forth in the restricted stock unit award agreement. At the time of grant, our Board may impose such restrictions or conditions on the award of restricted stock units that delay delivery to a date following the vesting of the award. Additionally, dividend equivalents may be paid or credited in respect of shares of Common Stock covered by a restricted stock unit award. Except as otherwise provided in the applicable award agreement, or other written agreement between us and the recipient, restricted stock unit awards that have not vested will be forfeited once the participant's continuous service ends for any reason.

Restricted Stock Awards

Restricted stock awards will be granted under restricted stock award agreements adopted by our Board. A restricted stock award may be awarded in consideration for cash, check, bank draft or money order, past services to us or any of our affiliates, or any other form of legal consideration that may be acceptable to our Board and permissible under applicable law. Our Board will determine the terms and conditions of restricted stock awards, including vesting and forfeiture terms. Dividends may be paid or credited with respect to shares subject to a restricted stock award, as determined by our Board and specified in the applicable restricted stock award agreement. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of Common Stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

Stock Appreciation Rights

Stock appreciation rights will be granted under stock appreciation right agreements adopted by our Board and denominated in shares of Common Stock equivalents. The terms of separation stock appreciation rights need not be identical. Our Board will determine the purchase price or strike price for a stock appreciation right, which generally will not be less than 100% of the fair market value of Common Stock on the date of grant. A stock appreciation right granted under the 2023 Plan will vest at the rate specified in the stock appreciation right agreement as will be determined by our Board. Stock appreciation rights may be settled in cash or shares of Common Stock (or any combination of Common Stock and cash) or in any other form of payment, as determined by our Board and specified in the stock appreciation right agreement.

Our Board will determine the term of stock appreciation rights granted under the 2023 Plan, up to a maximum of ten years. If a participant's service relationship with us or any of our affiliates ceases for any reason other than cause, disability, or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. If a participant's service relationship with us or any of our affiliates ceases due to death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested stock appreciation rights for a period of 18 months following the date of death. If a participant's service relationship with us or any of our affiliates ceases due to disability, the participant may generally exercise any vested stock appreciation rights for a period of 12 months following the cessation of service. In the event of a termination for cause, stock appreciation rights generally terminate upon the termination date. A holder of a stock appreciation right may not exercise a stock appreciation right at any time that the issuance of shares upon such exercise would violate applicable law. Unless provided otherwise in the stock appreciation right agreement or other written agreement between the participant and us, if a participant's service relationship with us or any of our affiliates ceases for any reason other than for cause and, at any time during the last thirty days of the applicable post-termination exercise period: (i) the exercise of the participant's stock appreciation right would be prohibited solely because the issuance of shares upon such exercise would violate applicable law, or (ii) the immediate sale of any shares issued upon such exercise would violate our trading policy, then the applicable post-termination exercise period will be extended to the last day of the calendar month that begins after the date the award would otherwise expire, with an additional extension of the exercise period to the last day of the next calendar month to apply if any of the foregoing restrictions apply at any time during such extended exercise period. There is no limitation as to the maximum permitted number of extensions. However, in no event may a stock appreciation right be exercised beyond the expiration of its term.

Other Stock Awards

Our Board will be permitted to grant other awards, based in whole or in part by reference to, or otherwise based on, Common Stock, either alone or in addition to other awards. Our Board will have the sole and complete discretion to determine the persons to whom and the time or times at which other stock awards will be granted, the number of shares under the other stock award (or cash equivalent) and all other terms and conditions of such awards.

Non-Employee Director Compensation Limit

The aggregate value of all compensation granted or paid following the effective date of the 2023 Plan to any individual for service as a non-employee director with respect to any fiscal year, including awards granted under the 2023 Plan (valued based on the grant date fair value for financial reporting purposes) and cash fees paid by us to such non-employee director, will not exceed $750,000 in total value, except such amount will increase to $1,000,000 for the year in which a non-employee director is first appointed or elected to our Board.

Changes to Capital Structure

In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, our Board will appropriately and proportionately adjust (i) the class(es) and maximum number of shares subject to the 2023 Plan and the maximum number of shares by which the share reserve may annually increase pursuant to the 2023 Plan; (ii) the class(es) and maximum number of shares that may be issued on the exercise of ISOs; and (iii) the class(es) and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding awards granted under the 2023 Plan.

Corporate Transactions

In the event of a corporate transaction (as defined below), unless otherwise provided in a participant’s award agreement or other written agreement with us or one of our affiliates or unless otherwise expressly provided by our Board at the time of grant, any awards outstanding under the 2023 Plan may be assumed, continued or substituted for, in whole or in part, by any surviving or acquiring corporation (or its parent company), and any reacquisition or repurchase rights held by us with respect to Common Stock issued pursuant to awards may be assigned to the successor (or its parent company). If the surviving or acquiring corporation (or its parent company) does not assume, continue or substitute for such awards, then (i) with respect to any such awards that are held by participants whose continuous service has not terminated prior to the effective time of the corporate transaction, or current participants, the vesting (and exercisability, if applicable) of such awards will be accelerated in full (or, in the case of awards with performance-based vesting with multiple vesting levels depending on the level of performance, unless provided otherwise in the applicable award agreement, vesting will accelerate at 100% of the target level) to a date prior to the effective time of the corporate transaction (contingent upon the effectiveness of the corporate transaction) as our Board determines (or, if our Board does not determine such a date, to the date that is five days prior to the effective time of the corporate transaction), and such awards will terminate if not exercised (if applicable) at or prior to the effective time of the corporate transaction, and any reacquisition or repurchase rights held by us with respect to such awards will lapse (contingent upon the effectiveness of the corporate transaction); and (ii) any such awards that are held by persons other than current participants will terminate if not exercised (if applicable) prior to the occurrence of the corporate transaction, except that any reacquisition or repurchase rights held by us with respect to such awards will not terminate and may continue to be exercised notwithstanding the corporate transaction.

In the event an award will terminate if not exercised prior to the effective time of a corporate transaction, our Board may provide, in its sole discretion, that the holder of such award may not exercise such award but instead will receive a payment, in such form as may be determined by our Board, equal in value to the excess (if any) of (i) the value of the property the participant would have received upon the exercise of the award, over (ii) any per share exercise price payable by such holder, if applicable. As a condition to the receipt of an award, a participant will be deemed to have agreed that the award will be subject to the terms of any agreement under the 2023 Plan governing a corporate transaction involving us.

Under the 2023 Plan, a “corporate transaction” generally will be the consummation, in a single transaction or in a series of related transactions, of (i) a sale or other disposition of all or substantially all, as determined by our Board, of the consolidated assets of us and our subsidiaries; (ii) a sale or other disposition of at least 50% of our outstanding securities; (iii) a merger, consolidation or similar transaction following which we are not the surviving corporation; or (iv) a merger, consolidation or similar transaction following

which we are the surviving corporation but the shares of Common Stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction.

Transferability

Except as expressly provided in the 2023 Plan or the form of award agreement, awards granted under the 2023 Plan may not be transferred or assigned by a participant. After the vested shares subject to an award have been issued, or in the case of a restricted stock award and similar awards, after the issued shares have vested, the holder of such shares is free to assign, hypothecate, donate, encumber or otherwise dispose of any interest in such shares provided that any such actions are in compliance with the provisions herein, the terms of our trading policy and applicable law.

Clawback/Recovery

All awards granted under the 2023 Plan will be subject to recoupment in accordance with any clawback policy that we are required to adopt pursuant to the listing standards of any national securities exchange or association on which our securities are listed or as is otherwise required by the Dodd-Frank Act or other applicable law and any clawback policy that we otherwise adopt, to the extent applicable and permissible under applicable law. In addition, our Board may impose such other clawback, recovery or recoupment provisions in an award agreement as our Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired shares of Common Stock or other cash or property upon the occurrence of cause.

Amendment or Termination

Our Board may accelerate the time at which an award granted under the 2023 Plan may first be exercised or the time during which an award grant under the 2023 Plan or any part thereof will vest, notwithstanding the provisions in the award agreement stating the time at which it may first be exercised or the time during which it will vest. Our Board will have the authority to amend, suspend, or terminate the 2023 Plan at any time, provided that such action does not materially impair the existing rights of any participant without such participant’s written consent. Certain material amendments will also require the approval of our stockholders. No ISOs may be granted after the tenth anniversary of the date our Board adopts the 2023 Plan. No awards may be granted under the 2023 Plan while it is suspended or after it is terminated.

Certain U.S. Federal Income Tax Aspects of Awards under the 2023 Plan

The following is a general summary under current law of the material federal income tax consequences to participants in the 2023 Plan under U.S. law. This summary deals with the general tax principles that apply and is provided only for general information. Certain types of taxes, such as state and local income taxes and taxes imposed by jurisdictions outside the United States, are not discussed. Tax laws are complex and subject to change and may vary depending on individual circumstances and from locality to locality. The summary does not discuss all aspects of income taxation that may be relevant to a participant in light of his or her personal investment circumstances and this summarized tax information is not tax advice.

Section 162(m) of the Internal Revenue Code

We will be entitled to a tax deduction in connection with an award under the 2023 Plan only in an amount equal to the ordinary income realized by the participant at the time the participant recognizes the income. Section 162(m) of the Internal Revenue Code places a limit of $1 million on the amount of compensation that we may deduct as a business expense in any year with respect to certain of our most highly paid executive officers. While our Board considers the deductibility of compensation as one factor in determining executive compensation, our Board retains the discretion to pay compensation (including through the issuance of awards) that is not deductible as it believes that it is in the best interests of our stockholders to maintain flexibility in our approach to executive compensation and to structure a program that we consider to be the most effective in attracting, motivating and retaining key employees.

Stock Options

A participant will not recognize taxable income at the time an option is granted, and we will not be entitled to a tax deduction at that time. A participant will recognize compensation taxable as ordinary income (and subject to income tax withholding in respect of

an employee) upon exercise of an NSO equal to the excess of the fair market value of the shares purchased over their purchase price, and we will be entitled to a corresponding deduction, except to the extent the deduction limits of Section 162(m) of the Internal Revenue Code apply. A participant will not recognize income (except for purposes of the alternative minimum tax) upon exercise of an ISO. If the shares acquired by exercise of an ISO are held for at least two years from the date the option was granted and one year from the date it was exercised, any gain or loss arising from a subsequent disposition of those shares will be taxed as long-term capital gain or loss, and we will not be entitled to any deduction. If, however, such shares are disposed of within either of the above-described periods, then in the year of that disposition, the participant will recognize compensation taxable as ordinary income equal to the excess of the lesser of (i) the amount realized upon that disposition, and (ii) the excess of the fair market value of those shares on the date of exercise over the exercise price, and we will be entitled to a corresponding deduction, except to the extent the deduction limits of Section 162(m) of the Internal Revenue Code apply.

Stock Appreciation Rights

A participant will not recognize taxable income at the time a stock appreciation right is granted, and we will not be entitled to a tax deduction at that time. Upon exercise, the participant will recognize compensation taxable as ordinary income (and subject to income tax withholding in respect of an employee) in an amount equal to the fair market value of any shares delivered and the amount of cash paid upon settlement. This amount is deductible by us as a compensation expense, except to the extent the deduction limits of Section 162(m) of the Internal Revenue Code apply.

Restricted Stock

A participant will not recognize taxable income at the time restricted stock is granted, and we will not be entitled to a tax deduction at that time, unless the participant makes an election to be taxed at that time. If such an election is made, the participant will recognize compensation taxable as ordinary income (and subject to income tax withholding in respect of an employee) at the time of the grant in an amount equal to the excess of the fair market value for the shares of Common Stock at such time over the amount, if any, paid for those shares of Common Stock. If such election is not made, the participant will recognize compensation taxable as ordinary income (and subject to income tax withholding in respect of an employee) at the time the restrictions constituting a substantial risk of forfeiture lapse in an amount equal to the excess of the fair market value of the shares of Common Stock at such time over the amount, if any, paid for those shares of Common Stock. The amount of ordinary income recognized by making the above-described election or upon the lapse of restrictions is deductible by us as compensation expense, except to the extent the deduction limits of Section 162(m) of the Internal Revenue Code apply.

Restricted Stock Units

A participant will not recognize taxable income at the time that restricted stock units are granted, and we will not be entitled to a tax deduction at that time. Upon settlement of restricted stock units, the participant will recognize compensation taxable as ordinary income (and subject to income tax withholding in respect of an employee) in an amount equal to the fair market value of any shares of Common Stock or other consideration delivered and the amount of any cash paid by us. The amount of ordinary income recognized is deductible by us as compensation expense, except to the extent the deduction limits of Section 162(m) of the Internal Revenue Code apply.

Other Stock Awards

The tax consequences associated with any other stock award will vary depending on the specific terms of such award. Among the relevant factors are whether or not the award has a readily ascertainable fair market value, whether or not the award is subject to forfeiture provisions or restrictions on transfer, the nature of the property to be received by the participant under the award, and the participant’s holding period and tax basis for the award or underlying shares of Common Stock.

The tax consequences for equity awards outside of the United States may differ significantly from the U.S. federal income tax consequences described above.

Orchestra BioMed, Inc. 2018 Stock Incentive Plan

General

The purposes of the 2018 Plan were (i) to attract and retain the best available personnel to ensure Legacy Orchestra's success and accomplish its goals; (ii) to incentivize employees, directors, and consultants with long-term, equity-based compensation to align their interests with the interests of Legacy Orchestra's stockholders; and (iii) to promote the success of Legacy Orchestra's business. The Legacy Orchestra Board and its stockholders approved the 2018 Plan on August 7, 2018, and it became effective immediately. The 2018 Plan provided for grants of incentive and nonqualified stock options, restricted and unrestricted stock awards and restricted stock unit awards, or collectively, stock awards, to Legacy Orchestra employees, directors or consultants or the employees, directors, and consultants of Legacy Orchestra's affiliates; *provided, however*, incentive stock options could be granted only to Legacy Orchestra employees or employees of its subsidiary corporations as required under Section 422 of the Internal Revenue Code. In connection with the Business Combination, following the effectiveness of the 2023 Plan, no further equity awards may be granted under the 2018 Plan. However, the 2018 Plan will continue to govern outstanding awards granted thereunder.

As of October 6, 2023, a total of 3,801,892 shares of Common Stock were subject to outstanding awards under the 2018 Plan.

Administration

The compensation committee our Board (or, in lieu of its compensation committee, the entire Board) will administer the 2018 Plan. Subject to the provisions of the 2018 Plan, the administrator will have the power to administer the 2018 Plan and make all determinations deemed necessary or advisable for administering the 2018 Plan, such as the power to select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2018 Plan, determine the terms and conditions of awards (such as the exercise price, the times or times at which the awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions, and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of the 2018 Plan and awards granted under it, to prescribe, amend, and rescind rules relating to the 2018 Plan, including creating sub-plans, and to modify or amend each award, such as the discretionary authority to extend the post-termination exercisability period of awards (provided that no option will be extended past its original maximum term). The administrator also will have the authority to institute an exchange program pursuant to which outstanding options are bought out for a payment in cash or shares, based on such terms and conditions as the administrator may establish. The administrator's decisions, interpretations, and other actions will be final and binding on all participants. The 2018 Plan is governed by Delaware law and includes provisions to assure compliance with applicable data privacy laws.

Stock Options

Both incentive stock options and nonqualified stock options may be granted under the 2018 Plan. Options granted to U.S. taxpayers must have an exercise price no less than 100% of fair market value of the covered shares of common stock on the date of grant, unless the options have a fixed exercise date, and a maximum ten-year term. For incentive stock options granted to any participant who owns more than 10% of the voting power of all classes of Orchestra's outstanding stock, the term must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 12 months. If termination is for cause, the option will immediately expire and may not be exercised. In all other cases, the option will generally remain exercisable for 90 days following the termination of service. Notwithstanding those periods, in no event may an option be exercised later than the expiration of its term. Subject to the provisions of the 2018 Plan, the administrator determines the other terms of options.

Restricted and Unrestricted Stock

Restricted and unrestricted stock may be granted under the 2018 Plan. Restricted stock awards are grants of shares of Orchestra Common Stock that vest in accordance with terms and conditions established by the administrator whereas unrestricted stock awards are fully vested on grant. The administrator will determine the number of shares of restricted or unrestricted stock granted to any employee, director or consultant and, subject to the provisions of the 2018 Plan, will determine the terms and conditions of such

awards. In the case of restricted stock awards, the administrator may impose whatever conditions for lapse of the restriction on the shares it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to Orchestra); *provided, however*, that the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to the restriction, unless the administrator provides otherwise. Shares of restricted stock as to which the restrictions have not lapsed are subject to Orchestra's right of repurchase or forfeiture.

Restricted Stock Units

Restricted stock units may be granted under the 2018 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of common stock. Subject to the provisions of the 2018 Plan, the administrator will determine the terms and conditions of restricted stock units, including the vesting criteria (which may include accomplishing specified performance criteria or continued service to Orchestra) and the form and timing of payment. Notwithstanding the foregoing, the administrator, in its sole discretion, may accelerate the time at which any restricted stock units will vest.

Transferability

Unless the administrator provides otherwise, the 2018 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. If the administrator makes an award transferable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Adjustments upon Certain Events

In the event of certain changes in Orchestra's capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the 2018 Plan, the administrator will adjust the number and class of shares that may be delivered under the 2018 Plan and/or the number, class and price of shares covered by each outstanding award and the numerical share limits set forth in the 2018 Plan. In general, in the event of Orchestra's proposed liquidation or dissolution, all awards will terminate immediately prior to the consummation of such proposed transaction.

Change in Control

The 2018 Plan provides that in the event of a change in control, as defined under the 2018 Plan, each outstanding award will be treated as the administrator determines, without obtaining the approval of Orchestra stockholders or any participant's consent. Such treatment may include vesting acceleration, settlement, cash-out, or termination of awards, or such other treatment as the administrator may determine. The administrator is not required to treat all awards, all awards held by a participant, or all awards of the same type, similarly.

Forfeiture and Clawback

All awards granted under the 2018 Plan will be subject to recapture or reimbursement to the extent the participant benefitted from financial results that were subsequently the subject of a material financial restatement. In addition, awards are subject to termination, recission or recapture in the event the participant misuses Orchestra's confidential or proprietary information or violates specified restrictive covenants.

Amendment, Termination

The administrator will have the authority to amend, suspend or terminate the 2018 Plan provided such action will not impair the existing rights of any participant. The 2018 Plan will automatically terminate in 2028, unless we terminate it sooner.

Defined Contribution Plan

Orchestra currently maintains a 401(k) retirement savings plan, or the 401(k) plan, for its employees, including its named executive officers, who satisfy certain eligibility requirements. The 401(k) plan is intended to qualify as a tax-qualified plan under Section 401(k) of the Internal Revenue Code. Orchestra's named executive officers are eligible to participate in the 401(k) plan on the

same basis as its other employees. The Internal Revenue Code allows eligible employees to defer a portion of their compensation, within prescribed limits, on a pre-tax basis through contributions to the 401(k) plan. Orchestra reserves the right to make discretionary matching contributions or non-elective contributions under the 401(k) plan. In 2021 and 2022, Orchestra did not provide a matching contribution or a non-elective contribution under the 401(k) plan.

Orchestra does not maintain any defined benefit pension plans.

Nonqualified Deferred Compensation

Orchestra does not maintain any nonqualified deferred compensation plans.

Director Compensation

Legacy Orchestra has historically provided equity-based compensation to certain of its directors for the time and effort necessary to serve as a member of the Orchestra Board.

Director Compensation Table

The following table presents summary information regarding the total compensation that was awarded to, earned by or paid to Orchestra's non-employee directors for services rendered during the year ended December 31, 2022.

Name	Year	Fees Earned or Paid in Cash ($)	Option Awards ($)[1] Year	Stock Awards ($)[1]	All other compensation ($)	Total ($)
Eric S. Fain, M.D.[2]	2022	18,000 [3]	101,862	14,177	60,000[4]	194,039
Eric A. Rose, M.D.[5]	2022	15,450 [6]	108,888		—	124,338
Geoffrey W. Smith[7]	2022	16,350 [8]	101,862	14,177	—	132,389
Jason M. Aryeh[9]	2022	17,400 [10]	101,862	14,177	—	133,439
Pamela Y. Connealy[11]	2022	18,000 [12]	101,862	14,177	—	134,039

(1) The amounts shown in this column represent the aggregate grant date fair value of option awards and stock awards granted to Orchestra's non-employee directors computed in accordance with FASB ASC 718. Such grant-date fair value does not take into account any estimated forfeitures related to service-vesting conditions. See Note 10 to Orchestra's consolidated audited financial statements for the fiscal years ended December 31, 2022 and 2021 included elsewhere in this prospectus for a description of Orchestra's assumptions used in the calculation.

(2) As of December 31, 2022, Dr. Fain held stock options covering 48,825 shares of common stock and 3,488 shares of restricted stock.

(3) Reflects Dr. Fain's board fees ($12,000) and fees for serving on the compensation committee ($1,950) and the nominating and corporate governance committee ($1,500) as well fees for serving as chairman of compensation committee ($2,550).

(4) Reflects consulting fees of $5,000 per month.

(5) As of December 31, 2022, Dr. Rose held stock options covering 52,313 shares of common stock and no shares of restricted stock.

(6) Reflects Dr. Rose's board fees ($12,000) and fees for serving on the compensation committee ($1,950) and the nominating and corporate governance committee ($1,500).

(7) As of December 31, 2022, Mr. Smith held stock options covering 48,825 shares of common stock and 3,488 shares of restricted stock.

(8) Reflects Mr. Smith's board fees ($12,000) and fees for serving on the audit committee ($2,400) and the compensation committee ($1,950).

(9) As of December 31, 2022, Mr. Aryeh held stock options covering 48,825 shares of common stock and 3,488 shares of restricted stock.

(10) Reflects Mr. Aryeh's board fees ($12,000) and fees for serving on the audit committee ($2,400) and the nominating and corporate governance committee ($1,500) as well fees for serving as chairman of the nominating and corporate governance committee ($1,500).

(11) As of December 31, 2022, Ms. Connealy held stock options covering 48,850 shares of common stock and 3,488 shares of restricted stock.

(12) Reflects Ms. Connealy's board fees ($12,000) and fees for serving on the audit committee ($2,400) as well fees for serving as chairperson of the audit committee ($3,600).

Director Compensation Policy

As of the date of this prospectus, our non-employee directors are entitled to the following compensation:

Cash Compensation

Annual Cash Compensation		Amount
Lead Independent Director	$	70,000
Board Members (other than Lead Independent Director)	$	40,000
Chair of the Audit Committee	$	20,000
Members of the Audit Committee (other than the Chairperson)	$	10,000
Chair of the Compensation Committee	$	15,000
Members of the Compensation Committee (other than the Chairperson)	$	7,500
Chair of the Nominating and Corporate Governance Committee	$	10,000
Members of the Nominating and Corporate Governance Committee (other than the Chairperson)	$	5,000

All annual cash compensation amounts for our non-employee directors are payable in equal quarterly installments in arrears, pro-rated for any partial months of service. Additionally, we will reimburse each non-employee director for reasonable, customary and documented travel expenses related to such director's attendance at Board and committee meetings.

Equity Compensation

For 2023, our non-employee directors were granted, at their election, either stock options or common stock or a combination thereof with a grant date fair value of between approximately $88,000 and $148,000, depending on their elections. These awards will vest in one installment on the one year anniversary of the grant date. Going forward, it is expected that, on the date of each annual meeting of the Company's stockholders (the "Annual Meeting"), each non-employee director automatically will be granted (i) a NSOs to purchase shares of Common Stock having a grant date fair value of $85,000, rounded down to the nearest whole share (the "Annual NSO Award"), and (ii) restricted stock units having a grant date fair value of $40,000, rounded down to the nearest whole share (the "Annual RSU Award" and, together with the Annual NSO Award, the "Annual Award"). Subject to adjustments, each Annual NSO Award and Annual RSU Award will vest in one installment on the earlier of (x) the one year anniversary of the grant date or (y) the following Annual Meeting. Each Annual NSO Award and Annual RSU Award will vest fully upon death, disability or a change in control, in each case, subject to the non-employee director's continued service through the applicable vesting date or change in control, as applicable.

Upon a non-employee director's appointment to the Board, such non-employee director automatically will be granted (i) a NSO to purchase shares of Common Stock having a grant date fair value of $85,000, rounded down to the nearest whole share (the "NSO Appointment Award"), (ii) Restricted Stock Units having a grant date fair value of $40,000, rounded down to the nearest whole share (the "RSU Appointment Award"), and (iii) to the extent applicable, a pro-rata portion of the Annual Award. Subject to adjustment, each NSO Appointment Award and RSU Appointment Award, including any pro-rata portions of the Annual Award, will vest in three equal, annual installments beginning with the first annual anniversary after the grant date. Each NSO Appointment Award and RSU Appointment Award will vest fully upon death, disability or a change in control, in each case, subject to the non-employee director's continued service through the applicable vesting date or change in control, as applicable.

Each non-employee director will have a maximum annual total compensation of $500,000, including both cash and equity, except that in the initial year of service or for a non-employee chairperson of the Board or the Lead Independent Director, the maximum annual total compensation will be $750,000.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

HSAC2

On June 11, 2020, HSAC2 sold an aggregate of 3,593,750 HSAC2 Ordinary Shares for $28,750 to the Sponsor. On August 3, 2020, HSAC2 declared a dividend of 0.113043478 shares for each outstanding share (an aggregate of 406,250 shares), resulting in an aggregate of 4,000,000 shares outstanding. This resulted in a purchase price of approximately $0.007 per HSAC2 Ordinary Share.

The Sponsor purchased, pursuant to a written purchase agreement with HSAC2, an aggregate of (i) 450,000 shares in a private placement simultaneously with the HSAC2 IPO (the "Private Shares") at $10.00 per HSAC2 Ordinary Share (for a total purchase price of $4,500,000) and (ii) 1,500,000 Private Warrants at $1.00 per warrant (for a total purchase price of $1,500,000). These purchases took place on a private placement basis simultaneously with the consummation of the HSAC2 IPO on August 6, 2020.

The Private Shares were identical to the HSAC2 Ordinary Shares sold in the HSAC2 IPO. However, the Sponsor HSAC2 Initial Shareholders agreed (A) to vote their 4,000,000 shares of Common Stock of the Company issued to the Sponsor and HSAC2's other initial shareholders (the "HSAC2 Initial Shareholders") prior to the HSAC2 IPO (the "Insider Shares"), Private Shares and any Public Shares in favor of any proposed business combination, (B) not to propose, or vote in favor of, prior to and unrelated to an initial business combination, an amendment to the HSAC2 amended and restated memorandum and articles of association that would affect the substance or timing of the ability of the holders of Public Shares to exercise redemption rights as described herein or of HSAC2's redemption obligation to redeem all Public Shares if it did not complete an initial business combination by February 6, 2023, unless it provided the holders of Public Shares, including the Initial Shareholders to the extent they purchased Public Shares (the 'Public Shareholders") an opportunity to redeem their Public Shares in conjunction with any such amendment, (C) not to redeem any shares, including Insider Shares, Private Shares and any Public Shares into the right to receive cash from the HSAC2 Trust Account in connection with a shareholder vote to approve a proposed initial business combination or sell any shares to HSAC2 in any tender offer in connection with a proposed initial business combination, and (D) that the Insider Shares and Private Shares shall not participate in any liquidating distribution upon winding up if a business combination is not consummated.

Each Private Warrant entitles the holder thereof to purchase one HSAC2 Ordinary Share at a price of $11.50 per HSAC2 Ordinary Share, subject to adjustment as provided therein. The Private Warrants became exercisable 30 days after the completion of the Business Combination and will expire five years after the completion of the Business Combination. Each Private Warrant will be non-redeemable and may be exercised on a cashless basis, in each case so long as they continue to be held by the Sponsor or its permitted transferees.

Additionally, the Sponsor agreed not to transfer, assign or sell any of the Private Shares, Private Warrants or underlying securities (except in limited circumstances) until the completion of the Business Combination.

The holders of Insider Shares issued and outstanding prior to the HSAC2 IPO, as well as the holders of the Private Shares and Private Warrants (and underlying securities), were entitled to certain registration rights prior to the consummation of the Business Combination. In connection with the Business Combination, we entered into the Amended and Restated Registration Rights Agreement with these persons. See "*Description of Securities—Amended and Restated Registration Rights and Lock-Up Agreement*."

The Sponsor agreed that, until the earlier of consummation of the Business Combination or liquidation, it would make available to HSAC2 certain general and administrative services, including office space, utilities and administrative support, as HSAC2 required from time to time. HSAC2 agreed to pay the Sponsor $10,000 per month for these services.

On June 11, 2020, the Sponsor loaned HSAC2 $300,000 to cover expenses related to the HSAC2 IPO. The loan was repaid without interest following the closing of the HSAC2 IPO.

Other than the fees described above, no compensation or fees of any kind, including finder's fees, consulting fees or other similar compensation, was paid to the HSAC2 Initial Shareholders or any of the members of HSAC2 management team, for services rendered to HSAC2 prior to, or in connection with the consummation of the Business Combination. However, such individuals received reimbursement for any out-of-pocket expenses incurred by them in connection with activities on HSAC2's behalf, such as identifying potential target businesses, performing business due diligence on suitable target businesses and business combinations as well as traveling to and from the offices, plants or similar locations of prospective target businesses to examine their operations. There was no limit on the amount of out-of-pocket expenses reimbursable by HSAC2; provided, however, that to the extent such expenses exceeded

the available proceeds not deposited in the HSAC2 Trust Account and the interest income earned on the amounts held in the HSAC2 Trust Account, such expenses would not be reimbursed by HSAC2 unless it consummated an initial business combination.

Orchestra

Described below are transactions and series of similar transactions, during Legacy Orchestra's last three fiscal years or currently proposed transactions in which:

- Legacy Orchestra has been or Orchestra is to be a participant;
- the amount involved exceeded or exceeds $120,000; and
- any of Legacy Orchestra's or Orchestra's directors, executive officers, or holders of more than 5% of its capital stock, or any immediate family member of, or person sharing the household with, any of these individuals, had or will have a direct or indirect material interest.

Other than as described below, there have not been, nor are there any currently proposed, transactions or series of similar transactions meeting this criteria to which Legacy Orchestra or Orchestra has been or will be a participant other than compensation arrangements, which are described where required under the sections titled "*Executive and Director Compensation*."

Convertible Preferred Stock Financings

Series B-1 Preferred Stock Private Placement

From April 15, 2019 through June 28, 2019, Legacy Orchestra issued an aggregate of 2,281,562 shares of Series B-1 Preferred Stock at a price of $15.00 per share, for total gross proceeds of approximately $34.2 million. All shares of Legacy Orchestra's Series B-1 Preferred Stock converted into shares of Legacy Orchestra Common Stock immediately prior to the closing of the closing of the Business Combination (the "Closing") in accordance with the Second Amended and Restated Certificate of Designations of Preferences, Rights and Limitations of Series B-1 Preferred Stock of Legacy Orchestra (the "Series B-1 Certificate of Designation"). On June 29, 2022, the Series B-1 Certificate of Designation was amended and restated to account for the subsequent authorization and issuance of the Series D-1 Preferred Stock and Series D-2 Preferred Stock, to incorporate mandatory conversion provisions that are also applicable to the Series D-1 Preferred Stock and Series D-2 Preferred Stock, and to increase the authorized number of shares of Series B-1 Preferred Stock, which increase was required in connection with the private placements of Series D-1 Preferred Stock and Series D-2 Preferred Stock.

Series D-1 Preferred Stock Private Placement

From March 3, 2022 through March 11, 2022, Legacy Orchestra issued an aggregate of 2,424,573 shares of Series D-1 Preferred Stock at a price of $11.25 per share, for total gross proceeds of approximately $27.3 million. All shares of Legacy Orchestra's Series D-1 Preferred Stock converted into shares of Legacy Orchestra Common Stock immediately prior to the Closing in accordance with the Second Amended and Restated Certificate of Designations of Preferences, Rights and Limitations of Series D-1 Preferred Stock of Legacy Orchestra (the "Series D-1 Certificate of Designation"). On June 29, 2022, the Series D-1 Certificate of Designation was amended and restated to effect a 2.419-for-1 forward stock split (the "Stock Split") of the Series D-1 Preferred Stock, to adjust (as a result of the Stock Split) the stated value of the Series D-1 Preferred Stock to $4.65 per share, to increase the authorized number of shares of Series D-1 Preferred Stock in connection with the Stock Split and to adjust the liquidation preferences of the Series D-1 Preferred Stock.

Series D-2 Preferred Stock Private Placement

On June 29, 2022, prior to any issuance of Series D-2 Preferred Stock, the Series D-2 Certificate of Designation (as defined below) was amended and restated to adjust the stated value of the Series D-2 Preferred Stock to $4.65 per share, to increase the authorized number of shares of Series D-2 Preferred Stock, and to adjust the liquidation preferences of the Series D-2 Preferred Stock. On June 30, 2022, Legacy Orchestra issued an aggregate of 17,753,263 shares of Series D-2 Preferred Stock at a price of $4.65 per share, for total gross proceeds of approximately $82.6 million. All shares of Legacy Orchestra's Series D-2 Preferred Stock converted into shares of Legacy Orchestra Common Stock immediately prior to the Closing in accordance with the Second Amended and Restated Certificate of Designations of Preferences, Rights and Limitations of Series D-2 Preferred Stock of Legacy Orchestra (the "Series D-2 Certificate of Designation").

Purchases of Legacy Orchestra by Persons Who Were Directors, Officers or Greater than 5% Beneficial Owners

The following table sets forth the aggregate number of shares of Legacy Orchestra capital stock acquired directly or indirectly by persons that were Legacy Orchestra's directors, officers or beneficial owners of more than 5% of its capital stock at the time of their purchases of Legacy Orchestra Common Stock.

Participant[1]	Series B-1 Preferred Stock	Series D-1 Preferred Stock	Series D-2 Preferred Stock	Purchase Price
Greater than 5% Stockholders				
Perceptive Life Sciences Master Fund, LLC[2]	266,667	—	1,612,904	$ 11,500,009
Medtronic, Inc.[3]	—	—	8,602,150	$ 39,999,998
Entities managed by RTW Investments, LP[4]	333,333	—	4,301,075	$ 24,999,994
First Riverside Investors LP[5]	—	1,612,904	537,634	$ 10,000,002
Directors and Executive Officers				
David Hochman[6]	—	54,929	—	$ 255,420
Darren Sherman[7]	—	—	5,378	$ 25,009
Jason Aryeh[8]	—	—	53,763	$ 250,000
Eric S. Fain[9]	1,300	20,322	—	$ 114,000

(1) Additional details regarding certain of these participants and their current equity holdings are provided in "*Security Ownership of Certain Beneficial Owners and Management*."

(2) Perceptive Life Sciences Master Fund, LLC ("Perceptive") purchased 266,667 shares of Series B-1 Preferred Stock in the Series B-1 Preferred Stock private placement offering for $4.0 million. Perceptive also purchased 1,612,904 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for $7.5 million.

(3) Medtronic, Inc. purchased 8,602,150 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for $40 million.

(4) Certain funds managed by RTW Investments, LP purchased 333,333 shares of Series B-1 Preferred Stock in the Series B-1 Preferred Stock private placement offering for $5.0 million. They also purchased 4,301,075 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for $20 million.

(5) First Riverside Investors LP ("First Riverside Investors") purchased 1,612,904 shares of Series D-1 Preferred Stock in the Series D-1 Preferred Stock Financing for $7.5 million. First Riverside Investors also purchased 537,634 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for $2.5 million.

(6) Mr. Hochman, through DPH 2008 Trust, purchased 54,929 shares of Series D-1 Preferred Stock in the Series D-1 Preferred Stock Financing for a total of $255,420.

(7) Mr. Sherman purchased 5,378 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for a total of $25,009.

(8) Mr. Aryeh purchased 53,763 shares of Series D-2 Preferred Stock in the Series D-2 Preferred Stock Financing for a total of $250,000.

(9) Dr. Fain, through Fain Living Trust, purchased 1,300 shares of Series B-1 Preferred Stock in the Series B-1 Preferred Stock private placement offering for a total of $19,500. He also purchased 20,322 shares of Series D-1 Preferred Stock in the Series D-1 Preferred Stock Financing for a total of $95,500.

Lease with Motus GI

In January 2020, Legacy Orchestra entered into an agreement for the use of portions of the premises of Motus GI for office space in Fort Lauderdale, Florida. The agreement will expire in November 2024. The monthly fee commenced on the month following the date of the agreement. Monthly fees will be between approximately $7,000 and $23,000 for the period from commencement through termination. The amount paid is estimated to be proportionate to the percentage of space used by Orchestra applied to the monthly rent obligated to be paid by Motus GI to its landlord. Pursuant to the agreement, Legacy Orchestra paid approximately $189,000 in the year ended December 31, 2021, approximately $245,000 in the year ended December 31, 2022, and Orchestra paid approximately $134,000 in the six months ended June 30, 2023. Mr. Hochman served as Chairman of the board of directors of Motus GI from December 2016 to April 2023 and remained a member of the board of directors until September 2023. Mr. Sherman also served on the board of directors of Motus GI from December 2016 to September 2023. In addition, Orchestra has a small minority equity investment in Motus GI.

Collaboration Agreement with Medtronic

On June 30, 2022, Legacy Orchestra entered into an exclusive license and collaboration agreement with Medtronic, which holds more than 5% of our Common Stock. For a discussion regarding the Medtronic Collaboration, see "*Business — BackBeat Cardiac Neuromodulation Product Candidate (CNT) — Strategic Collaboration Agreement with Medtronic*."

PRINCIPAL SECURITYHOLDERS

The following table sets forth information known to us regarding the beneficial ownership of our Common Stock as of October 6, 2023 by:

- each person or "group" (as such term is used in Section 13(d)(3) of the Exchange Act) known by us to be the beneficial owner of more than 5% of our Common Stock;
- each of our current executive officers and directors; and
- all of our current executive officers and directors as a group.

Beneficial ownership is determined according to the rules of the SEC, which generally provide that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power over that security, including options and warrants that are currently exercisable or exercisable within 60 days. Shares subject to options and warrants that are currently exercisable or exercisable within 60 days of October 6, 2023 are considered outstanding and beneficially owned by the person holding such options or warrants for the purpose of computing the percentage ownership of that person, but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

The beneficial ownership of our Common Stock is based on 35,743,972 shares of Common Stock issued and outstanding as of October 6, 2023.

Unless otherwise indicated in the footnotes to the table below, and subject to applicable community property laws, we believe that all persons named in the table below have sole voting and investment power with respect to their beneficially owned shares of Common Stock.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	% of Class
Directors and named executive officers[(1)]		
David P. Hochman[(2)]	893,975	2.5%
Darren R. Sherman[(3)]	801,902	2.2%
Michael D. Kaswan[(4)]	140,699	*
Jason Aryeh[(5)]	98,245	*
Pamela Y. Connealy[(6)]	32,532	*
Eric S. Fain, M.D.[(7)]	65,028	*
Eric A. Rose, M.D.[(8)]	39,174	*
Geoffrey W. Smith[(9)]	1,874,290	5.2%
All directors and executive officers as a group (eleven individuals)	4,145,297	11.0%
Five Percent Holders:		
HSAC 2 Holdings, LLC[(10)]	4,360,956	11.9%
Entities managed by RTW Investments, LP[(11)]	5,620,645	15.7%
Medtronic, Inc.[(12)]	5,868,916	16.4%
Perceptive Life Sciences Master Fund[(13)]	2,432,089	6.8%

* Less than one percent.

(1) Unless otherwise indicated, the business address of each of the following individuals is 150 Union Square Drive, New Hope, PA 18938.

(2) Consists of (i) 165,498 shares held directly by Mr. Hochman; (ii) 62,502 shares held by the DPH 2008 Trust, over which Mr. Hochman has sole voting and dispositive power; (ii) 3,823 shares held by the NSH 2008 Family Trust (the "NSH Trust"), over which Mr. Hochman has sole voting

and dispositive power; (iv) 534,910 shares Mr. Hochman has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly; (v) 127,242 shares DPH 2008 Trust has the right to acquire within 60 days of October 6, 2023 upon the exercise of options it holds.

(3) Consists of (i) 83,778 shares held directly by Mr. Sherman; and (ii) 718,124 shares Mr. Sherman has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly.

(4) Consists of (i) 76,511 shares held directly by Mr. Kaswan; and (ii) 64,188 shares Mr. Kaswan has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly.

(5) Consists of (i) 62,984 shares held directly by Mr. Aryeh; and (ii) 35,261 shares Mr. Aryeh has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly.

(6) Consists of (i) 4,246 shares held directly by Ms. Connealy; and (ii) 28,286 shares Ms. Connealy has the right to acquire within 60 days of October 6, 2023 upon the exercise of options she holds directly.

(7) Consists of (i) 29,767 shares held by the Fain Living Trust (the "Fain Trust"), over which Mr. Fain has sole voting and dispositive power; and (ii) 35,261 shares the Fain Trust has the right to acquire within 60 days of October 6, 2023 upon the exercise of options it holds.

(8) Consists of (i) 2,169 shares held directly by Mr. Rose; and (ii) 37,005 shares Mr. Rose has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly.

(9) Consists of (i) 4,246 shares held directly by Mr. Smith; (ii) 35,261 shares Mr. Smith has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly; (iii) 1,277,297 shares held by Ascent Biomedical Ventures II, L.P. ("ABV II"), (iv) 312,406 shares held by Ascent Biomedical Ventures Synecor, LP ("ABV Synecor"); and (v) 245,080 shares held by Ascent Biomedical Ventures II NY, LP ("ABV II NY"). ABV, LLC serves as general partner to ABV II, ABV Synecor and ABV II NY. Mr. Smith is a managing member of ABV, LLC. As such, Mr. Smith may be deemed to have voting and dispositive power over the shares held by ABV II, ABV Synecor and ABV II NY.

(10) Consists of 4,360,956 held by HSAC 2 Holdings, LLC. HSAC 2 Holdings, LLC is governed by a board of directors consisting of three directors: Roderick Wong, Naveen Yalamanchi, and Alice Lee. Each director has one vote, and the approval of a majority of the directors is required to approve an action of HSAC 2 Holdings, LLC. Under the so-called "rule of three," if voting and dispositive decisions regarding an entity's securities are made by three or more individuals, and a voting or dispositive decision requires the approval of a majority of those individuals, then none of the individuals is deemed a beneficial owner of the entity's securities. Based upon the foregoing analysis, no director of HSAC 2 Holdings, LLC exercises voting or dispositive control over any of the shares held by HSAC 2 Holdings, LLC, even those in which he or she directly holds a pecuniary interest. Accordingly, none of them will be deemed to have or share beneficial ownership of the shares held by HSAC 2 Holdings, LLC. The principal business address of HSAC 2 Holdings, LLC is 40 10th Avenue, Floor 7, New York, NY 10014.

(11) Consists of (i) 2,263,336 shares of Common Stock held by RTW Innovation Master Fund, Ltd.; (ii) 2,762,705 shares of Common Stock held by RTW Master Fund, Ltd.; and (iii) 594,604 shares of Common Stock held by RTW Biotech Opportunities Fund Ltd (together with RTW Innovation Master Fund, Ltd. and RTW Master Fund, Ltd., the "RTW Funds"). Roderick Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments, LP. Both he and RTW Investments, LP may be deemed the beneficial owner of the shares held by the RTW Funds and each disclaims beneficial ownership except to the extent of their pecuniary interest in the holders. The principal business address of the RTW Funds is 40 10th Avenue, Floor 7, New York, NY 10014.

(12) Consists of 5,868,916 shares held by Covidien Group S.à.r.l. The principal address of Covidien Group S.à.r.l. is c/o Medtronic, Inc., Operational Headquarters, 710 Medtronic Parkway, Minneapolis, MN 55432-5604.

(13) Consists of 2,432,089 shares held by Perceptive Life Sciences Master Fund, Ltd. ("Perceptive"). Perceptive Advisors LLC ("Perceptive Advisors") serves as the investment manager to the Perceptive and may be deemed to beneficially own such shares. Joseph Edelman is the managing member of Perceptive Advisors and may be deemed to have voting and dispositive power over the shares held by Perceptive. The principal business address of Perceptive is 51 Astor Place, 10th Floor, New York, NY 10003.

SELLING SECURITYHOLDERS

This prospectus also relates to the offer and sale from time to time, upon the expiration of lock-up agreements, if applicable, by:

(a) the Selling Stockholders of up to an aggregate of 22,221,440 Resale Shares, consisting of:

  (i) up to 10,675,809 Orchestra Affiliate Shares;

  (ii) up to 10,070,645 Sponsor Shares;

  (iii) up to 22,279 shares of Common Stock issued to certain selling stockholders in May 2023 in connection with the exercise of Company warrants;

  (iv) up to 750,000 HSAC2 Warrant Shares;

  (v) up to 675,000 Officer and Director Warrant Shares;

  (vi) up to 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company; and

(b) the Selling Warrantholder of up to 750,000 HSAC2 Warrants.

A description of our relationships with certain of the Selling Securityholders and their affiliates is set forth in "*Certain Relationships and Related Party Transactions*."

Certain of the Selling Securityholders, including the Sponsor and its affiliates, certain shareholders of HSAC2 prior to the Business Combination, certain equityholders of Legacy Orchestra and our executive officers and directors, are subject to lock-up agreements with respect to the Resale Shares and the Warrants, including the Common Stock issuable upon exercise of the Warrants. Certain of the Selling Securityholders have agreed, subject to certain customary exceptions, not to sell, assign, offer to sell, contract or agree to sell, grant any option to purchase or otherwise dispose of or agree to dispose of, directly or indirectly, any shares of Common Stock or any security convertible into or exercisable or exchanged for Common Stock for 12 months following the Closing (with our officers and directors and Medtronic subject to a 24-month lock-up following the Closing and Terumo subject to a lock-up until the commercial launch of Virtue). All of the Resale Shares and HSAC2 Warrants sold in this offering will become eligible for sale upon expiration of the applicable lock-up period or release by competent parties, except for any shares held by our affiliates, as such term is defined in Rule 144 under the Securities Act.

We cannot advise you as to whether the Selling Securityholders will in fact sell any or all of such shares of Common Stock or whether the Selling Warrantholder will sell any of the HSAC2 Warrants. In particular, the Selling Securityholders identified below may have sold, transferred or otherwise disposed of all or a portion of their securities after the date on which they provided us with information regarding their securities in transactions exempt from registration under the Securities Act.

Unless otherwise indicated in the footnotes below, no Selling Securityholder has had any material relationship with us or any of our affiliates within the past three years other than as a securityholder.

The following table sets forth certain information provided by or on behalf of the Selling Securityholders as of October 6, 2023 concerning the Resale Shares and Warrants that may be offered from time to time by each Selling Securityholder with this prospectus. See *"Plan of Distribution."* For the purposes of this following table, we have assumed that the Selling Securityholders will have sold all of the securities covered by this prospectus upon the completion of the offering.

Beneficial ownership is determined according to the rules of the SEC, which generally provide that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power over that security, including options and warrants that are currently exercisable or exercisable within 60 days. Shares subject to options and warrants that are currently exercisable or exercisable within 60 days of October 6, 2023 are considered outstanding and beneficially owned by the person holding

such options or warrants for the purpose of computing the percentage ownership of that person, but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

The percentage ownership of voting securities in the following table is based on 35,743,972 shares of our Common Stock issued and outstanding as of October 6, 2023.

	Beneficial Ownership of Common Stock Prior to the Offering					Beneficial Ownership of Common Stock After the Offered Shares are Sold		Beneficial Ownership of Warrants After the Offered Warrants are Sold	
Name and Address of Selling Securityholder[1]	**Number of Shares of Common Stock**	**% of Class**	**Warrants Beneficially Owned Prior to the Offering**	**Number of Shares of Common Stock Being Offered**	**Warrants Being Offered**	**Number of Shares**	**Percent**	**Number of Warrants**	**Percent**
HSAC2 Holdings, LLC[2]	5,110,956	14.0 %	750,000	5,110,956	750,000	—	—	—	—
RTW Master Fund, Ltd.[3]	2,762,705	7.7 %	—	2,762,705	—	—	—	—	—
RTW Innovation Master Fund, Ltd.[4]	2,263,336	6.3 %	—	2,263,336	—	—	—	—	—
RTW Biotech Opportunities Fund Ltd[5]	594,604	1.7 %	—	594,604	—	—	—	—	—
Ascent Biomedical Ventures II, L.P.[6]	1,277,297	3.6 %	—	1,277,297	—	—	—	—	—
Ascent Biomedical Ventures II NY, LP[6]	245,080	*	—	245,080	—	—	—	—	—
Ascent Biomedical Ventures Synecor, LP[6]	312,406	*	—	312,406	—	—	—	—	—
Avenue Venture Opportunities Fund, L.P.[7]	37,716	*	25,542	5,542	—	32,174	*	—	—
Avenue Venture Opportunities Fund II, L.P.[8]	150,860	*	102,165	22,165	—	128,695	*	—	—
Covidien Group S.a.r.l.[9]	5,868,916	16.4 %	—	5,868,916	—	—	—	—	—
Perceptive Life Sciences Master Fund[10]	2,432,089	6.8 %	—	2,432,089	—	—	*	—	—
Pedro Granadillo[11]	22,261	*	—	22,261	—	—	*	—	—
Stuart Peltz[12]	22,261	*	—	22,261	—	—	*	—	—
Michael Brophy[13]	22,261	*	—	22,261	—	—	*	—	—
Carsten Boess[14]	22,261	*	—	22,261	—	—	*	—	—
David P. Hochman[15]	893,875	2.5 %	225,000	456,823	—	662,152	1.8 %	—	—
Darren R. Sherman[16]	801,902	2.2 %	225,000	308,778	—	718,124	2.0 %	—	—
Michael D. Kaswan[17]	140,699	*	—	76,511	—	64,188	*	—	—
Yuval Mika[18]	309,089	*	50,000	99,572	—	259,517	*	—	—
Fain Living Trust[19]	65,028	*	15,000	44,767	—	35,261	*	—	—
Eric Rose[20]	39,174	*	15,000	17,169	—	37,005	*	—	—
Jason Aryeh[21]	98,245	*	15,000	77,984	—	35,261	*	—	—
Pamela Connealy[22]	32,532	*	15,000	19,246	—	28,286	*	—	—
Geoffrey Smith[23]	1,874,290	5.2 %	15,000	54,507	—	35,261	*	—	—
George Papandreou, Ph.D.[24]	31,062	*	50,000	50,000	—	31,062	*	—	—
Hans-Peter Stoll, M.D., Ph.D.[25]	23,248	*	50,000	50,000	—	23,248	*	—	—
Angelo Auricchio[26]	1,086	*	—	1,086	—	—	*	—	—
Barry Katzen[27]	2,325	*	—	2,325	—	—	*	—	—
Gary Pruden[28]	2,325	*	—	2,325	—	—	*	—	—
Gregg Stone[29]	2,325	*	—	2,325	—	—	*	—	—
John Barr[30]	2,325	*	—	2,325	—	—	*	—	—
Louis Shapiro[31]	2,168	*	—	2,168	—	—	*	—	—
Robert S. Schwartz[32]	2,325	*	—	2,325	—	—	*	—	—
Roger de la Torre[33]	2,325	*	—	2,325	—	—	*	—	—

* Less than 1%.

(1) Unless otherwise indicated, the business address of each of the Selling Securityholders is 150 Union Square Drive, New Hope, PA 18938.

(2) Common Stock beneficially owned prior to the offering consists of (i) 4,360,956 shares held by HSAC 2 Holdings, LLC and (ii) 750,000 shares over which HSAC 2 Holdings, LLC has the right to acquire within 60 days of October 6, 2023 upon the exercise warrants held by HSAC 2 Holdings, LLC. HSAC 2 Holdings, LLC is governed by a board of directors consisting of three directors: Roderick Wong, Naveen Yalamanchi, and Alice Lee. Each director has one vote, and the approval of a majority of the directors is required to approve an action of HSAC 2 Holdings, LLC. Under the so-called "rule of three," if voting and dispositive decisions regarding an entity's securities are made by three or more individuals, and a voting or dispositive decision requires the approval of a majority of those individuals, then none of the individuals is deemed a beneficial owner of the entity's securities. Based upon the foregoing analysis, no director of HSAC 2 Holdings, LLC exercises voting or dispositive control over any of the shares held by HSAC 2 Holdings, LLC, even those in which he or she directly holds a pecuniary interest.

Accordingly, none of them will be deemed to have or share beneficial ownership of the shares held by HSAC 2 Holdings, LLC. The principal business address of HSAC 2 Holdings, LLC is 40 10th Avenue, Floor 7, New York, NY 10014.

(3) Common Stock beneficially owned prior to the offering consists of 2,762,705 shares of held by RTW Master Fund, Ltd. Roderick Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments, LP. Both he and RTW Investments, LP may be deemed the beneficial owner of the shares held by RTW Investments, L.P. and each disclaims beneficial ownership except to the extent of their pecuniary interest in the holders. The principal business address of RTW Master Fund, Ltd. is 40 10th Avenue, Floor 7, New York, NY 10014.

(4) Common Stock beneficially owned prior to the offering consists of 2,263,336 shares held by RTW Innovation Master Fund, Ltd. Roderick Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments, LP. Both he and RTW Investments, LP may be deemed the beneficial owner of the shares held by RTW Innovation Master Fund, Ltd. and each disclaims beneficial ownership except to the extent of their pecuniary interest in the holders. The principal business address of RTW Innovation Master Fund, Ltd. is 40 10th Avenue, Floor 7, New York, NY 10014.

(5) Common Stock beneficially owned prior to the offering consists of 594,604 shares held by RTW Biotech Opportunities Fund Ltd. Roderick Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments, LP. Both he and RTW Investments, LP may be deemed the beneficial owner of the shares held by RTW Biotech Opportunities Fund Ltd and each disclaims beneficial ownership except to the extent of their pecuniary interest in the holders. The principal business address of RTW Biotech Opportunities Fund Ltd is 40 10th Avenue, Floor 7, New York, NY 10014.

(6) Geoffrey Smith has voting and dispositive power of the shares held by this entity. See footnote (23).

(7) Common Stock beneficially owned prior to the offering consists of (i) 12,174 shares held by Avenue Venture Opportunities Fund, L.P ("Avenue I") and (ii) 25,542 shares over which Avenue I has the right to acquire within 60 days of October 6, 2023 upon the exercise warrants held by Avenue I. Avenue Venture Opportunities Partners, LLC is the general partner of the Avenue I. GL Venture Opportunities Partners I LLC is the managing member of Avenue Venture Opportunities Partners, LLC. Marc Lasry is the managing member of GL Venture Opportunities Partners I, LLC. As such, Mr. Lasry may be deemed to have voting and dispositive power over the shares held by Avenue I. Mr. Lasry disclaims beneficial ownership of the securities held by Avenue I, except to the extent of his pecuniary interest in Avenue I. The principal business address of Avenue I is 11 West 42nd Street, Floor 9, New York, NY 10036.

(8) Common Stock beneficially owned prior to the offering consists of (i) 48,695 shares held by Avenue Venture Opportunities Fund II, L.P ("Avenue II") and (ii) 102,165 shares over which Avenue II has the right to acquire within 60 days of October 6, 2023 upon the exercise warrants held by Avenue II. Avenue Venture Opportunities Partners II LLC is the general partner of the Avenue II. GL Venture Opportunities Partners II, LLC is the managing member of Avenue Venture Opportunities Partners II LLC. Marc Lasry is the managing member of GL Venture Opportunities Partners II, LLC. As such, Mr. Lasry may be deemed to have voting and dispositive power over the shares held by Avenue II. Mr. Lasry disclaims beneficial ownership of the securities held by Avenue II, except to the extent of his pecuniary interest in Avenue II. The principal business address of Avenue II is 11 West 42nd Street, Floor 9, New York, NY 10036.

(9) Common Stock beneficially owned prior to the offering consists of 5,868,916 shares held by Covidien Group S.à.r.l. The principal business address of Covidien Group S.à.r.l. is c/o Medtronic, Inc., Operational Headquarters, 710 Medtronic Parkway, Minneapolis, MN 55432-5604.

(10) Common Stock beneficially owned prior to the offering consists of 2,432,089 shares directly held by Perceptive Life Sciences Master Fund, Ltd. ("Perceptive"). Perceptive Advisors LLC ("Perceptive Advisors") serves as the investment manager to the Perceptive and may be deemed to beneficially own such shares. Joseph Edelman is the managing member of Perceptive Advisors and may be deemed to have voting and dispositive power over the shares held by Perceptive. The principal business address of Perceptive is 51 Astor Place, 10th Floor, New York, NY 10003.

(11) Common Stock beneficially owned prior to the offering consists of 22,261 shares held directly by Mr. Granadillo. Mr. Grandillo has a principal business address of 40 10th Avenue, Floor 7, New York, NY 10014.

(12) Common Stock beneficially owned prior to the offering consists of 22,261 shares held directly by Mr. Peltz. Mr. Peltz has a principal business address of 40 10th Avenue, Floor 7, New York, NY 10014.

(13) Common Stock beneficially owned prior to the offering consists of 22,261 shares held directly by Mr. Brophy. Mr. Brophy has a principal business address of 40 10th Avenue, Floor 7, New York, NY 10014.

(14) Common Stock beneficially owned prior to the offering consists of 22,261 shares held directly by Mr. Boess. Mr. Boess has a principal business address of 40 10th Avenue, Floor 7, New York, NY 10014.

(15) Common Stock beneficially owned prior to the offering consists of (i) 165,498 shares held directly by Mr. Hochman; (ii) 62,502 shares held by the DPH 2008 Trust, over which Mr. Hochman has sole voting and dispositive power; (ii) 3,823 shares held by the NSH 2008 Family Trust (the "NSH Trust"), over which Mr. Hochman has sole voting and dispositive power; (iv) 534,910 shares Mr. Hochman has the right to acquire within

60 days of October 6, 2023 upon the exercise of options he holds directly; (v) 127,242 shares DPH 2008 Trust has the right to acquire within 60 days of October 6, 2023 upon the exercise of options. Warrants beneficially owned prior to the offering consists of 225,000 Officer and Director Warrants, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(16) Common Stock beneficially owned prior to the offering consists of (i) 83,778 shares held directly by Mr. Sherman; and (ii) 718,124 shares Mr. Sherman has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 225,000 Officer and Director Warrants held directly by Mr. Sherman, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(17) Common Stock beneficially owned prior to the offering consists of (i) 76,511 shares held directly by Mr. Kaswan; and (ii) 64,188 shares Mr. Kaswan has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly.

(18) Common Stock beneficially owned prior to the offering consists of (i) 49,572 shares held directly by Mr. Mika; (ii) 259,517 shares Mr. Mika has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 50,000 Officer and Director Warrants held directly by Mr. Mika, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(19) Common Stock beneficially owned prior to the offering consists of (i) 29,767 shares held by the Fain Living Trust (the “Fain Trust”), over which Mr. Fain has sole voting and dispositive power; and (ii) 35,261 shares the Fain Trust has the right to acquire within 60 days of October 6, 2023 upon the exercise of options it holds. Warrants beneficially owned prior to the offering consists of 15,000 Officer and Director Warrants held directly by Mr. Fain, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(20) Common Stock beneficially owned prior to the offering consists of (i) 2,169 shares held directly by Mr. Rose; and (ii) 37,005 shares Mr. Rose has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 15,000 Officer and Director Warrants held directly by Mr. Rose, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(21) Common Stock beneficially owned prior to the offering consists of (i) 62,984 shares held directly by Mr. Aryeh; and (ii) 35,261 shares Mr. Aryeh has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 15,000 Officer and Director Warrants held directly by Mr. Aryeh, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(22) Common Stock beneficially owned prior to the offering consists of (i) 4,246 shares held directly by Ms. Connealy; and (ii) 28,286 shares Ms. Connealy has the right to acquire within 60 days of October 6, 2023 upon the exercise of options she holds directly. Warrants beneficially owned prior to the offering consists of 15,000 Officer and Director Warrants held directly by Ms. Connealy, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(23) Common Stock beneficially owned prior to the offering consists (i) 4,246 shares held directly by Mr. Smith; (ii) 35,261 shares Mr. Smith has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly; (iii) 1,277,297 shares held by Ascent Biomedical Ventures II, L.P. (“ABV II”), (iv) 312,406 shares held by Ascent Biomedical Ventures Synecor, LP (“ABV Synecor”); and (v) 245,080 shares held by Ascent Biomedical Ventures II NY, LP (“ABV II NY”). ABV, LLC serves as general partner to ABV II, ABV Synecor and ABV II NY. Mr. Smith is a managing member of ABV, LLC. As such, Mr. Smith may be deemed to have voting and dispositive power over the shares held by ABV II, ABV Synecor and ABV II NY. Warrants beneficially owned prior to the offering consists of 15,000 Officer and Director Warrants held directly by Mr. Smith, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(24) Common Stock beneficially owned prior to the offering consists of 31,062 shares Mr. Papandreou has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 50,000 Officer and Director Warrants held directly by Mr. Papandreou, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(25) Common Stock beneficially owned prior to the offering consists of 23,248 shares Mr. Stoll has the right to acquire within 60 days of October 6, 2023 upon the exercise of options he holds directly. Warrants beneficially owned prior to the offering consists of 50,000 Officer and Director Warrants held directly by Mr. Stoll, 50% of which will vest and become exercisable on January 26, 2025 and the remaining 50% will vest and become exercisable on January 26, 2026.

(26) Common Stock beneficially owned prior to the offering consists of 1,086 shares held directly by Mr. Auricchio. Mr. Auricchio has a principal business address of Via Bellavista 11A, CH-6977 Ruvigliana, Switzerland.

(27) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. Katzen. Mr. Katzen has a principal business address of 1125 San Pedro Ave, Coral Gables, FL, 33156.

(28) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. Pruden. Mr. Pruden has a principal business address of 2 Tines Field Path, Newtown, PA 18940.

(29) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. Stone. Mr. Stone has a principal business address of 21 Wyckham Hill Lane, Greenwich, CT, 06831.

(30) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. Barr. Mr. Barr has a principal business address of PO Box 655, Ogunquit, ME, 03907.

(31) Common Stock beneficially owned prior to the offering consists of 2,168 shares held directly by Mr. Shapiro. Mr. Shapiro has a principal address business of 5718 Walnut Street, Pittsburgh, PA 15232.

(32) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. Schwartz. Mr. Schwartz has a principal address of 4127 Gulf of Mexico Dr. #N202, Longboat Key, FL, 34228.

(33) Common Stock beneficially owned prior to the offering consists of 2,325 shares held directly by Mr. de la Torre. Mr. de la Torre has a principal address of 2328 W. 127th St., Leawood, KS 66209.

PLAN OF DISTRIBUTION

We are registering the issuance by us of up to an aggregate of 1,932,841 Warrant Shares, consisting of up to:

(a) 750,000 HSAC2 Warrant Shares;

(b) 675,000 Officer and Director Warrant Shares; and

(c) 507,841 Orchestra Warrant Shares.

We are also registering for resale from time to time by:

(a) the Selling Stockholders of up to an aggregate of up to 22,221,440 Resale Shares, consisting of:

 (i) up to 10,675,809 Orchestra Affiliate Shares;

 (ii) up to 10,070,645 Sponsor Shares;

 (iii) up to 22,279 shares of Common Stock issued to certain selling stockholders in May 2023 in connection with the exercise of Company warrants;

 (iv) up to 750,000 HSAC2 Warrant Shares;

 (v) up to 675,000 Officer and Director Warrant Shares;

 (vi) up to 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company; and

(b) the Selling Warrantholder of up to 750,000 HSAC2 Warrants.

We will not receive any proceeds from the sale by the Selling Securityholders of the securities offered by them described in this prospectus, except with respect to amounts received by us upon the exercise of the Warrants for cash. The aggregate proceeds to the Selling Securityholders will be the purchase price of the securities less any discounts and commissions borne by the Selling Securityholders.

The Selling Securityholders will pay any underwriting discounts and commissions and expenses incurred by the Selling Securityholders for brokerage, accounting, tax or legal services or any other expenses incurred by the Selling Securityholders in disposing of the securities. We are required to pay all other fees and expenses incident to the registration of the securities to be offered and sold pursuant to this prospectus.

The shares of Common Stock and the Warrants beneficially owned by the Selling Securityholders covered by this prospectus may be offered and sold from time to time by the Selling Securityholders. The term “Selling Securityholders” includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from a Selling Securityholder as a gift, pledge, partnership distribution or other transfer.

The Selling Securityholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions. Each Selling Securityholder reserves the right to accept and, together with its respective agents, to reject, any proposed purchase of securities to be made directly or through agents. The Selling Securityholders and any of their permitted transferees may sell their securities offered by this prospectus on any stock exchange, market or trading facility on which the securities are traded or in private transactions. If underwriters are used in the sale, such underwriters will acquire the shares for their own account. These sales may be at a fixed price or varying prices, which may be changed, or at market prices prevailing at the time of sale, at prices relating to prevailing market prices or at negotiated prices. The

securities may be offered to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. The obligations of the underwriters to purchase the securities will be subject to certain conditions.

The Selling Securityholders may sell their Resale Shares and HSAC2 Warrants by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the offered securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of Nasdaq;
- through trading plans entered into by a Selling Securityholder pursuant to Rule 10b5-1 under the Exchange Act, that are in place at the time of an offering pursuant to this prospectus and any applicable prospectus supplement hereto that provide for periodic sales of their securities on the basis of parameters described in such trading plans;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- agreements with broker-dealers to sell a specified number of the securities at a stipulated price per share or warrant;
- in “at the market” offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or at prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents;
- in privately negotiated transactions;
- in options transactions;
- through a combination of any of the above methods of sale; or
- any other method permitted pursuant to applicable laws.

In addition, a Selling Securityholder that is an entity may elect to make a pro rata, in-kind distribution of securities to its members, partners or stockholders pursuant to the registration statement of which this prospectus is a part by delivering a prospectus with a plan of distribution. Such members, partners or stockholders would thereby receive freely tradeable securities pursuant to the distribution through a registration statement. To the extent a distributee is an affiliate of ours (or to the extent otherwise required by law), we may file a prospectus supplement in order to permit the distributees to use the prospectus to resell the securities acquired in the distribution.

There can be no assurance that the Selling Securityholders will sell all or any of the securities offered by this prospectus. In addition, any shares that qualify for sale pursuant to Rule 144 may be sold under Rule 144 rather than pursuant to this prospectus. The Selling Securityholders have the sole and absolute discretion not to accept any purchase offer or make any sale of securities if they deem the purchase price to be unsatisfactory at any particular time.

Subject to the terms of the agreement(s) governing the registration rights applicable to a Selling Securityholder’s shares of Common Stock or Warrants, such Selling Securityholder may transfer shares of Common Stock or Warrants to one or more “permitted transferees” in accordance with such agreements and, if so transferred, such permitted transferee(s) will be the selling beneficial owner(s) for purposes of this prospectus. Upon being notified by a Selling Securityholder that it intends to sell our

securities, we will, to the extent required, promptly file a supplement to this prospectus to name specifically such person as a Selling Securityholder.

With respect to a particular offering of the securities held by the Selling Securityholders, to the extent required, an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement of which this prospectus is part, will be prepared and will set forth, to the extent required, the following information:

- the specific securities to be offered and sold;
- the names of the Selling Securityholders;
- the respective purchase prices and public offering prices, the proceeds to be received from the sale, if any, and other material terms of the offering;
- settlement of short sales entered into after the date of this prospectus;
- the names of any participating agents, broker-dealers or underwriters, if not already named herein; and
- any applicable commissions, discounts, concessions and other items constituting compensation from the Selling Securityholders.

In connection with distributions of the Resale Shares or otherwise, the Selling Securityholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of shares of Common Stock in the course of hedging transactions, broker-dealers or other financial institutions may engage in short sales of shares of Common Stock in the course of hedging the positions they assume with Selling Securityholders. The Selling Securityholders may also sell shares of Common Stock short and redeliver the shares to close out such short positions. The Selling Securityholders may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The Selling Securityholders may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged shares pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In order to facilitate the offering of the securities offered by this prospectus, any underwriters or agents, as the case may be, involved in the offering of such securities may engage in transactions that stabilize, maintain or otherwise affect the price of our securities. Specifically, the underwriters or agents, as the case may be, may over-allot in connection with the offering, creating a short position in our securities for their own account. In addition, to cover overallotments or to stabilize the price of our securities, the underwriters or agents, as the case may be, may bid for, and purchase, such securities in the open market. Finally, in any offering of securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allotted to an underwriter or a broker-dealer for distributing such securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. The underwriters or agents, as the case may be, are not required to engage in these activities, and may end any of these activities at any time.

The Selling Securityholders may solicit offers to purchase the securities directly from, and may sell such securities directly to, institutional investors or others. In this case, no underwriters or agents would be involved. The terms of any of those sales, including the terms of any bidding or auction process, if utilized, will be described in the applicable prospectus supplement.

It is possible that one or more underwriters may make a market in our securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for our securities. Our shares of Common Stock are currently listed on the Nasdaq Global Market under the symbol “OBIO.” Our Warrants are not listed on any exchange.

The Selling Securityholders may authorize underwriters, broker-dealers or agents to solicit offers by certain purchasers to purchase the securities at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts

providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions the Selling Securityholders pay for solicitation of these contracts.

A Selling Securityholder may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by any Selling Securityholder or borrowed from any Selling Securityholder or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from any Selling Securityholder in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment). In addition, any Selling Securityholder may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

In effecting sales, broker-dealers or agents engaged by the Selling Securityholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the Selling Securityholders in amounts to be negotiated immediately prior to the sale.

If at the time of any offering made under this prospectus a member of FINRA participating in the offering has a “conflict of interest” as defined in FINRA Rule 5121 (“Rule 5121”), that offering will be conducted in accordance with the relevant provisions of Rule 5121.

To our knowledge, there are currently no plans, arrangements or understandings between the Selling Securityholders and any broker-dealer or agent regarding the sale of the securities by the Selling Securityholders. Upon our notification by a Selling Securityholder that any material arrangement has been entered into with an underwriter or broker-dealer for the sale of securities through a block trade, special offering, exchange distribution, secondary distribution or a purchase by an underwriter or broker-dealer, we will file, if required by applicable law or regulation, a supplement to this prospectus pursuant to Rule 424(b) under the Securities Act disclosing certain material information relating to such underwriter or broker-dealer and such offering.

Underwriters, broker-dealers or agents may facilitate the marketing of an offering online directly or through one of their affiliates. In those cases, prospective investors may view offering terms and a prospectus online and, depending upon the particular underwriter, broker-dealer or agent, place orders online or through their financial advisors.

In offering the shares covered by this prospectus, the Selling Securityholders and any broker-dealers who execute sales for the Selling Securityholders may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. Any discounts, commissions, concessions or profit they earn on any resale of those securities may be underwriting discounts and commissions under the Securities Act.

In order to comply with the securities laws of certain states, if applicable, the shares must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

We have advised the Selling Securityholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the Selling Securityholders and their affiliates. In addition, we will make copies of this prospectus available to the Selling Securityholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The Selling Securityholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

A holder of Warrants may exercise its Warrants in accordance with the applicable warrant agreement on or before the expiration date set forth therein by surrendering to the Company the certificate evidencing such Warrant, with the form of election to purchase set forth thereon, properly completed and duly executed, accompanied by full payment of the exercise price and any and all applicable taxes due in connection with the exercise of the Warrant, subject to any applicable provisions relating to cashless exercises in accordance with the applicable warrant agreement.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following is a discussion of certain material U.S. federal income tax consequences relating to the ownership and disposition of our Common Stock and Warrants, which we collectively refer to as our “securities.” This discussion is limited to certain U.S. federal income tax considerations for investors that will acquire our securities for cash after the effective time of the Business Combination and will hold them as capital assets within the meaning of Section 1221 of the Internal Revenue Code and that acquire our Common Stock and Warrants for cash pursuant to this prospectus.

This discussion is a summary only and does not describe all of the tax consequences that may be relevant to you in light of your particular circumstances, including but not limited to the alternative minimum tax, the special tax accounting rules under Section 451(b) of the Internal Revenue Code, the Medicare tax on certain net investment income and the different consequences that may apply if you are subject to special rules that apply to certain types of investors, including but not limited to:

- banks, financial institutions or financial services entities;
- broker-dealers;
- governments or agencies or instrumentalities thereof;
- regulated investment companies;
- real estate investment trusts;
- expatriates or former long-term residents of the United States;
- persons that actually or constructively own five percent or more (by vote or value) of our shares;
- persons that acquired our securities pursuant to an exercise of employee share options, in connection with employee share incentive plans or otherwise as compensation;
- insurance companies;
- dealers or traders subject to a mark-to-market method of accounting with respect to our securities;
- persons holding our securities as part of a “straddle,” constructive sale, hedge, wash sale, conversion or other integrated or similar transaction;
- persons holding our securities in connection with a trade or business conducted outside the United States;
- U.S. holders (as defined below) whose functional currency is not the U.S. dollar;
- partnerships (or entities or arrangements classified as partnerships or other pass-through entities for U.S. federal income tax purposes) and any beneficial owners of such partnerships;
- tax-exempt entities;
- controlled foreign corporations; and
- passive foreign investment companies.

If a partnership (including an entity or arrangement treated as a partnership or other pass-thru entity for U.S. federal income tax purposes) holds our securities, the tax treatment of a partner, member or other beneficial owner in such partnership will generally

depend upon the status of the partner, member or other beneficial owner, the activities of the partnership and certain determinations made at the partner, member or other beneficial owner level. If you are a partner, member or other beneficial owner of a partnership holding our securities, you are urged to consult your tax advisor regarding the tax consequences of the purchase, ownership and disposition of our securities.

This discussion is based on the Internal Revenue Code, administrative pronouncements, judicial decisions, and final, temporary and proposed Treasury Regulations as of the date hereof, which are subject to change, possibly on a retroactive basis, and changes to any of which subsequent to the date of this prospectus may affect the tax consequences described herein. This discussion does not address any aspect of state, local or non-U.S. taxation, or any U.S. federal taxes other than income taxes (such as gift and estate taxes).

We have not sought, and do not expect to seek, a ruling from the U.S. Internal Revenue Service (the "IRS") as to any U.S. federal income tax consequence described herein. The IRS may disagree with the discussion herein, and its determination may be upheld by a court. Moreover, there can be no assurance that future legislation, regulations, administrative rulings or court decisions will not adversely affect the accuracy of the statements in this discussion. You are urged to consult your tax advisor with respect to the application of U.S. federal tax laws to your particular situation, as well as any tax consequences arising under the laws of any state, local or foreign jurisdiction.

THIS DISCUSSION IS ONLY A SUMMARY OF CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS ASSOCIATED WITH THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR SECURITIES. EACH PROSPECTIVE INVESTOR IN OUR SECURITIES IS URGED TO CONSULT ITS OWN TAX ADVISOR WITH RESPECT TO THE PARTICULAR TAX CONSEQUENCES TO SUCH INVESTOR OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR SECURITIES, INCLUDING THE APPLICABILITY AND EFFECT OF ANY U.S. FEDERAL NON-INCOME, STATE, LOCAL, AND NON-U.S. TAX LAWS OR ANY APPLICABLE INCOME TAX TREATY.

U.S. Holders

This section applies to you if you are a "U.S. holder." A U.S. holder is a beneficial owner of our securities who or that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation) organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is includible in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust, if (i) a court within the United States is able to exercise primary supervision over the administration of the trust and one or more United States persons (as defined in the Internal Revenue Code) have authority to control all substantial decisions of the trust or (ii) it has a valid election in effect under Treasury Regulations to be treated as a United States person.

Taxation of Distributions

If we pay distributions in cash or other property (other than certain distributions of our stock or rights to acquire our stock) to U.S. holders of our Common Stock, such distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of current and accumulated earnings and profits will constitute a return of capital that will be applied against and reduce (but not below zero) the U.S. holder's adjusted tax basis in its Common Stock. Any remaining excess will be treated as gain realized on the sale or other disposition of its Common Stock and will be treated as described under "*U.S. Holders — Gain or Loss on Sale, Taxable Exchange or Other Taxable Disposition of Common Stock and Warrants*" below.

Dividends we pay to a U.S. holder that is treated as a taxable corporation generally will qualify for the dividends received deduction if the requisite holding period is satisfied. Dividends that exceed certain thresholds in relation to a corporate U.S. holder's tax basis in the stock could be characterized as an "extraordinary dividend" (as defined in Section 1059 of the Internal Revenue Code) subject to special rules. With certain exceptions (including, but not limited to, dividends treated as investment income for purposes of

investment interest deduction limitations), and provided certain holding period requirements are met, dividends we pay to a non-corporate U.S. holder may constitute “qualified dividend income” that will be subject to tax at preferential rates accorded to long-term capital gains. If the applicable holding period and other applicable requirements are not satisfied, then a corporation may not be able to qualify for the dividends received deduction and would have taxable income equal to the entire dividend amount. Likewise, if the applicable holding period and other applicable requirements are not satisfied, then non-corporate U.S. holders may be subject to tax on such dividend at regular ordinary income tax rates instead of the preferential rate that applies to qualified dividend income. Note that, it is unclear whether the redemption rights with respect to HSAC2 may prevent the holder period of Common Stock from commencing prior to the termination of such rights. U.S. holders should consult their tax advisors regarding the availability of the lower rate for any dividends paid with respect to our Common Stock.

Gain or Loss on Sale, Taxable Exchange or Other Taxable Disposition of Common Stock and Warrants.

Upon a sale or other taxable disposition of our Common Stock or Warrants, a U.S. holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. holder’s adjusted tax basis in its Common Stock or Warrants. Any such capital gain or loss generally will be long-term capital gain or loss if the U.S. holder’s holding period for its Common Stock or Warrants so disposed of exceeds one year. Long-term capital gains recognized by non-corporate U.S. holders may be eligible to be taxed at reduced rates. Note that, it is unclear whether the redemption rights with respect to HSAC2 may prevent the holder period of Common Stock from commencing prior to the termination of such rights. U.S. holders should consult their tax advisors regarding the availability of the lower rate for any dividends paid with respect to our Common Stock.

The deductibility of capital losses is subject to limitations.

Generally, the amount of gain or loss recognized by a U.S. holder is an amount equal to the difference between (i) the sum of the amount of cash and the fair market value of any property received in such disposition and (ii) the U.S. holder’s adjusted tax basis in its Common Stock or Warrants so disposed of. A U.S. holder’s adjusted tax basis in its Common Stock or Warrant generally will equal the U.S. holder’s acquisition cost less, in the case of a share of Common Stock, any prior distributions treated as a return of capital.

Exercise, Lapse, or Redemption of a Warrant

Except as discussed below with respect to the cashless exercise of a Warrant, a U.S. holder generally will not recognize gain or loss upon the exercise of a Warrant. A U.S. holder’s tax basis in a share of our Common Stock received upon exercise of the Warrant generally will be an amount equal to the sum of the U.S. holder’s initial investment in the Warrant and the exercise price. The U.S. holder’s holding period for the share of Common Stock received upon exercise of the Warrant generally will commence on the date of exercise of the Warrant or the date following the date of exercise of the Warrant; however, in either case the holding period will not include the period during which the U.S. holder held the Warrant. If a Warrant is allowed to lapse unexercised, a U.S. holder generally will recognize a capital loss equal to such holder’s tax basis in the Warrant.

The tax consequences of a cashless exercise of a Warrant are not clear under current tax law. A cashless exercise may be tax-free, either because the exercise is not a gain realization event or because the exercise is treated as a recapitalization for U.S. federal income tax purposes. In either tax-free situation, a U.S. holder’s basis in the share of Common Stock received would equal the holder’s basis in the Warrants used to effect the cashless exercise. If the cashless exercise is not treated as a gain realization event, a U.S. holder’s holding period in the Common Stock generally would be treated as commencing on the date of exercise of the Warrant or the date following the date of exercise of the Warrant; however, in either case the holding period will not include the period during which the U.S. holder held the Warrant. If the cashless exercise were treated as a recapitalization, the holding period of the Common Stock would include the holding period of the Warrant.

It is also possible that a cashless exercise could be treated in part as a taxable exchange in which gain or loss would be recognized. In such event, a portion of the Warrants to be exercised on a cashless basis could, for U.S. federal income tax purposes, be deemed to have been surrendered in consideration for the exercise price of the remaining Warrants, which would be deemed to be exercised. For this purpose, a U.S. holder could be deemed to have surrendered Warrants having an aggregate fair market value equal to the exercise price for the total number of Warrants to be deemed exercised. The U.S. holder would recognize capital gain or loss in an amount equal to the difference between the fair market value of the Warrants deemed surrendered and the U.S. holder’s tax basis in such Warrants. In this case, a U.S. holder’s tax basis in the Common Stock received would equal the sum of the U.S. holder’s initial investment in the Warrants deemed exercised and the exercise price of such Warrants. A U.S. holder’s holding period for the Common

Stock in such case generally would commence on the date following the date of exercise (or possibly the date of exercise) of the Warrant.

Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance which, if any, of the alternative tax consequences and holding periods described above would be adopted by the IRS or a court of law. Accordingly, U.S. holders should consult their tax advisors regarding the tax consequences of a cashless exercise.

Possible Constructive Distributions

The terms of each Warrant provide for an adjustment to the number of shares of Common Stock for which the Warrant may be exercised or to the exercise price of the Warrant in certain events as discussed in the section of this registration statement captioned "*Description of Securities — Outstanding Warrants*." An adjustment that has the effect of preventing dilution generally is not taxable. U.S. holders of the Warrants would, however, be treated as receiving a constructive distribution from us if, for example, the adjustment increases the Warrant holders' proportionate interest in our assets or earnings and profits (for instance, through an increase in the number of shares of Common Stock that would be obtained upon exercise or through a decrease in the exercise price of the Warrant) as a result of a taxable distribution of cash or other property (such as other securities) to the holders of our Common Stock. Such constructive distributions would be subject to tax as described under "*—Taxation of Distributions*" above in the same manner as if the U.S. holders of the Warrants received a cash distribution from us equal to the fair market value of such increased interest. Generally, a U.S. holder's adjusted tax basis in its Warrants should be increased to the extent of any constructive distribution treated as a dividend.

Information Reporting and Backup Withholding

In general, information reporting requirements may apply to distributions paid to a U.S. holder and to the proceeds of the sale or other disposition of our Common Stock, unless the U.S. holder is an exempt recipient. Backup withholding may apply to such payments if the U.S. holder fails to provide a taxpayer identification number, a certification of exempt status or has been notified by the IRS that it is subject to backup withholding (and such notification has not been withdrawn).

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided the required information is timely furnished to the IRS.

Non-U.S. Holders

This section applies to you if you are a "Non-U.S. holder." As used herein, the term "Non-U.S. holder" means a beneficial owner of our Common Stock or Warrants who or that is for U.S. federal income tax purposes:

- a non-resident alien individual (other than certain former citizens and residents of the United States subject to U.S. tax as expatriates);
- a foreign corporation; or
- an estate or trust that is not a U.S. holder;

but generally does not include individuals who are present in the United States for 183 days or more in the taxable year of the disposition of their securities. If you are such an individual, you should consult your tax advisor regarding the U.S. federal income tax consequences of the purchase, ownership or sale or other disposition of our securities.

Taxation of Distributions

In general, any distributions (other than certain distributions of our stock or rights to acquire our stock) we make to a Non-U.S. holder of our Common Stock, to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles), will constitute dividends for U.S. federal income tax purposes and, provided such dividends are not

effectively connected with the Non-U.S. holder's conduct of a trade or business within the United States, the gross amount of the dividend will be subject to withholding tax at a rate of 30%, unless such Non-U.S. holder is eligible for a reduced rate of withholding tax under an applicable income tax treaty and provides proper certification of its eligibility for such reduced rate (usually on an IRS Form W-8BEN or W-8BEN-E).

Any distribution not constituting a dividend will be treated first as reducing (but not below zero) the Non-U.S. holder's adjusted tax basis in its Common Stock and, to the extent such distribution exceeds the Non-U.S. holder's adjusted tax basis, as gain realized from the sale or other disposition of its Common Stock, which will be treated as described under "*Non-U.S. Holders — Gain on Sale, Taxable Exchange or Other Taxable Disposition of Common Stock and Warrants*" below.

The withholding tax generally does not apply to dividends paid to a Non-U.S. holder who provides an IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. holder's conduct of a trade or business within the United States. Instead, the effectively connected dividends will be subject to regular U.S. federal income tax as if the Non-U.S. holder were a U.S. resident, subject to an applicable income tax treaty providing otherwise. A corporate Non-U.S. holder receiving effectively connected dividends may also be subject to an additional "branch profits tax" imposed at a rate of 30% (or a lower applicable treaty rate).

Gain on Sale, Taxable Exchange or Other Taxable Disposition of Common Stock and Warrants

A Non-U.S. holder generally will not be subject to U.S. federal income or withholding tax in respect of gain recognized on a sale, taxable exchange or other taxable disposition of its Common Stock or Warrants (including an expiration of Warrants) unless:

- the gain is effectively connected with the conduct by the Non-U.S. holder of a trade or business within the United States (and, under an applicable income tax treaty, is attributable to a United States permanent establishment or fixed base maintained by the Non-U.S. holder); or

- we are or have been a "United States real property holding corporation" (a "USRPHC") for U.S. federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the Non-U.S. holder's holding period unless the relevant securities are regularly traded on an established securities market and certain other conditions are met.

Unless an applicable treaty provides otherwise, gain described in the first bullet point above will be subject to tax at generally applicable U.S. federal income tax rates as if the Non-U.S. holder were a U.S. resident. Any gains described in the first bullet point above of a Non-U.S. holder that is treated as a foreign corporation for U.S. federal income tax purposes may also be subject to an additional "branch profits tax" imposed at a 30% rate (or lower treaty rate). If the second bullet point above applies to a Non-U.S. holder, gain recognized by such holder on the sale, exchange or other disposition of its securities will be subject to tax at generally applicable U.S. federal income tax rates. We will be classified as a USRPHC if the fair market value of our "United States real property interests" equals or exceeds 50% of the sum of the fair market value of our worldwide real property interests plus our other assets used or held for use in a trade or business, as determined for U.S. federal income tax purposes. We believe we currently are not, and do not anticipate becoming, a USRPHC. However, because our status as a USPRHC depends on the composition our business assets, which may change, no assurance can be provided as to whether we would be treated as a USRPHC in any future year.

Exercise, Lapse, or Redemption of a Warrant

The characterization for U.S. federal income tax purposes of the exercise, redemption or lapse of a Warrant held by a Non-U.S. holder will generally correspond to the characterization described under "*—U.S. Holders—Exercise, Lapse, or Redemption of a Warrant*" above, although to the extent a cashless exercise or redemption results in a taxable exchange, the consequences would follow those described above in "*—Gain or Loss on Sale, Taxable Exchange, or Other Taxable Disposition of Common Stock and Warrants*."

Possible Constructive Distributions

The terms of each Warrant provide for an adjustment to the number of shares of Common Stock for which the Warrant may be exercised or to the exercise price of the Warrant in certain events as discussed in the section of this prospectus captioned "*Description*

Of Securities — Outstanding Warrants." An adjustment which has the effect of preventing dilution generally is not taxable. Non-U.S. holders of the Warrants would, however, be treated as receiving a constructive distribution from us if, for example, the adjustment increases the Warrant holders' proportionate interest in our assets or earnings and profits (for instance, through an increase in the number of shares of Common Stock that would be obtained upon exercise or through a decrease in the exercise price of the Warrant) as a result of a distribution of cash or other property such as other securities to the holders of shares of our Common Stock. Such constructive distribution to a Non-U.S. holder of Warrants would be treated as if such Non-U.S. holder had received a cash distribution from us equal to the fair market value of such increased interest (taxed as described above under "—*Taxation of Distributions*"). For certain informational reporting purposes, we are required to determine the date and amount of any such constructive distributions and publicly report such information or report such information to the IRS and holders of Warrants not exempt from information reporting. Proposed Treasury Regulations, which taxpayers may generally rely on prior to the issuance of final regulations, specify how the date and amount of constructive distributions are determined.

Information Reporting and Backup Withholding

Information returns generally will be filed with the IRS in connection with payments to a Non-U.S. holder of distributions on our Common Stock. Proceeds from a sale or other taxable disposition of our securities within the United States or conducted through certain U.S.-related brokers may be subject to backup withholding or information reporting unless a Non-U.S. holder complies with certification procedures to establish that it is not a United States person. The certification procedures required to claim a reduced rate of withholding under a treaty generally will satisfy such certification requirements. Proceeds of a disposition of our securities conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting. Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a Non-U.S. holder will be allowed as a credit against such holder's U.S. federal income tax liability and may entitle such holder to a refund, *provided that* the required information is timely furnished to the IRS.

FATCA Withholding Taxes

The Foreign Account Tax Compliance Act ("FATCA") imposes withholding of 30% on payments of dividends on our Common Stock (or constructive dividends, if any, with respect to our Warrants), or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our securities paid (or deemed paid) to "foreign financial institutions" (which is broadly defined for this purpose and in general includes investment vehicles) and certain other non-U.S. entities unless various U.S. information reporting and due diligence requirements (generally relating to ownership by United States persons of interests in or accounts with those entities) have been satisfied by, or an exemption applies to, the payee (typically certified as to by the delivery of a properly completed IRS Form W-8BEN-E or other applicable form). Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules. Under certain circumstances, a Non-U.S. holder might be eligible for refunds or credits of such withholding taxes, and a Non-U.S. holder might be required to file a U.S. federal income tax return to claim such refunds or credits. FATCA withholding was scheduled to apply to payments of gross proceeds from the sale or other disposition of property that produces U.S.-source interest or dividends beginning on January 1, 2019, but on December 13, 2018, the IRS released proposed regulations that, if finalized in their proposed form, would eliminate the obligation to withhold on gross proceeds. Such proposed regulations also delayed withholding on certain other payments received from other foreign financial institutions that are allocable, as provided for under final Treasury Regulations, to payments of U.S.-source dividends, and other fixed or determinable annual or periodic income. Although these proposed Treasury Regulations are not final, taxpayers generally may rely on them until final Treasury Regulations are issued. However, there can be no assurance that final Treasury Regulations will provide the same exceptions from FATCA withholding as the proposed Treasury Regulations. Prospective investors should consult their tax advisors regarding the effects of FATCA on their investment in securities.

DESCRIPTION OF SECURITIES

General

The following description summarizes the most important terms of our securities. The following summary does not purport to be complete and is subject to the Charter, the Bylaws and the provisions of applicable law. A copy of the Charter and a copy of the Bylaws are filed as exhibits to the registration statement of which this prospectus forms a part. The stockholders are encouraged to read the applicable provisions of the DGCL, the Charter and the Bylaws in their entirety for a complete description of the rights and preferences of our securities.

Authorized and Outstanding Stock

The Charter authorizes the issuance of (i) 340,000,000 shares of Common Stock, $0.0001 par value per share and (ii) 10,000,000 shares of preferred stock, $0.0001 par value per share (the “Preferred Stock”). As of October 6, 2023, there were 35,743,972 shares of Common Stock and no shares of Preferred Stock issued and outstanding.

Common Stock

The Charter provides the following with respect to the rights, powers, preferences and privileges of our Common Stock.

Voting Rights

Holders of our Common Stock are entitled to one vote per share of Common Stock held at all meetings of stockholders. The Charter does not provide for cumulative voting for the election of directors.

Dividend Rights

Subject to preferences that may be applicable to any outstanding preferred stock, the holders of our Common Stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by the Board, out of funds legally available therefor.

Rights upon Liquidation

In the event of our liquidation, dissolution or winding up, the holders of our Common Stock will be entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock, if any, then outstanding.

No Preemptive or Similar Rights

Holders of our Common Stock have no redemption, conversion or preemptive rights. There are no sinking fund provisions applicable to our Common Stock.

Fully Paid and Non-Assessable

The outstanding shares of our Common Stock are fully paid and non-assessable.

Preferred Stock

As of the date of this prospectus, there are no shares of Preferred Stock outstanding. Pursuant to the Charter, our Board has the authority to issue undesignated Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences and the number of shares constituting any series or the designation of such series, without further vote or action by the stockholders.

The issuance of Preferred Stock may have the effect of delaying, deferring or preventing a change in control without further action by the stockholders and may adversely affect the voting and other rights of the holders of our Common Stock. At present, we have no plans to issue any of the Preferred Stock.

Outstanding Warrants

As of October 6, 2023, there are outstanding warrants to acquire up to an aggregate of 1,960,548 shares of Common Stock.

HSAC2 Warrants

There are currently outstanding an aggregate of 750,000 HSAC2 Warrants.

Each HSAC2 Warrant entitles the registered holder to purchase one share of Common Stock at a price of $11.50 per share, subject to adjustment as described in this prospectus, at any time commencing 30 days after the completion of the Business Combination. The HSAC2 Warrants have a net exercise provision under which its holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of the Common Stock at the time of exercise of the HSAC2 Warrants after deduction of the aggregate exercise price. The HSAC2 Warrants will expire five years after the date on which they first became exercisable, at 5:00 p.m., New York City time.

None of the HSAC2 Warrants will be redeemable by us.

If the number of outstanding shares of Common Stock is increased by a stock dividend payable in shares of Common Stock, then, on the effective date of such stock dividend, or split-up or similar event, the number of shares issuable on exercise of each HSAC2 Warrant will be increased in proportion to such increase in the outstanding shares.

If the number of outstanding shares is decreased by a consolidation, combination, reverse share split or reclassification of Common Stock or other similar event, then, on the effective date of such consolidation, combination, reverse share split, reclassification or similar event, the number of shares issuable on exercise of each HSAC2 Warrant will be decreased in proportion to such decrease in outstanding shares of Common Stock.

Whenever the number of shares of Common Stock issuable upon the exercise of the HSAC2 Warrants is adjusted, as described above, the HSAC2 Warrant exercise price will be adjusted by multiplying the HSAC2 Warrant exercise price immediately prior to such adjustment by a fraction (x) the numerator of which will be the number of shares purchasable upon the exercise of the warrants immediately prior to such adjustment and (y) the denominator of which will be the number of shares so purchasable immediately thereafter.

If, at any time while an HSAC2 Warrant is outstanding, (i) we effect any merger or consolidation with or into another person, (ii) we effect any sale of all or substantially all of our assets or a majority of the Common Stock is acquired by a third party, in each case, in one or a series of related transactions, (iii) any tender offer or exchange offer is completed pursuant to which all or substantially all of the holders of Common Stock are permitted to tender or exchange their shares for other securities, cash or property, or (iv) we effect any reorganization or reclassification of Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property (in any such case, a “Fundamental Transaction”), then the holder of an HSAC2 Warrant shall have the right thereafter to receive, upon exercise of the HSAC2 Warrant, the same amount and kind of securities, cash or property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of the number of shares of Common Stock then issuable upon exercise in full of such HSAC2 Warrant.

Officer and Director Warrants

There were formerly 1,500,000 HSAC2 Warrants. As part of the Business Combination, the Sponsor forfeited 50% of its HSAC2 Warrants, comprising 750,000 HSAC2 Warrants, for no consideration, immediately prior to the Closing. Pursuant to the terms of the Merger Agreement, immediately following such forfeiture and prior to the Closing, HSAC2 issued 750,000 Officer and Director Warrants to eleven specified employees and directors of Legacy Orchestra. These Officer and Director Warrants have substantially similar terms to the forfeited HSAC2 Warrants, except that they will become exercisable between 24 and 36 months after the Closing.

Legacy Orchestra Warrants that Converted into Orchestra Warrants

At the effective time of the Business Combination, each warrant to purchase shares of Legacy Orchestra Common Stock that was outstanding and unexercised immediately prior to the effective time of the Business Combination was assumed by Orchestra and represented a warrant to purchase shares of Common Stock on the same terms and subject to the same conditions (including as to vesting and exercisability) as were in effect with respect to such warrants immediately prior to such effective time, with appropriate adjustments to the number of shares of Common Stock underlying such warrant and the exercise price applicable thereto to account for the Business Combination.

Warrants Issued in the Formation Mergers

- Warrants to purchase an aggregate of 87,916 shares of Common Stock at an exercise price of $10.22 per share, which Legacy Orchestra issued on May 31, 2018 in connection with the mergers entered into with each of Caliber Therapeutics, Inc., BackBeat Medical, Inc. and FreeHold Surgical, Inc. pursuant to which Legacy Orchestra was formed in exchange for Caliber and BackBeat warrants that had been issued to designees of Aegis with respect to Aegis serving as a placement agent in Caliber and Backbeat capital-raising transactions. Among other things, these warrants have a six-year term that begins on January 26, 2023 and become exercisable one year after the closing of the Business Combination.

Warrants Issued to Designees of Aegis Capital for Serving as Placement Agent in Connection with Legacy Orchestra's Series B Preferred Stock and Series B-1 Preferred Stock Financings

- Warrants to purchase an aggregate of 319,925 shares of Common Stock at an exercise price of $10.22 per share, which Legacy Orchestra issued to designees of Aegis pursuant to the Placement Agency Agreement entered into with Aegis in connection with Legacy Orchestra's offerings of Series B Preferred Stock and Series B-1 Preferred Stock. Among other things, these warrants have a six-year term that begins on January 26, 2023 and become exercisable one year after the closing of the Business Combination.

Provisions Applicable to All of the Above Orchestra Warrants

All of the warrants above:

- provide for the adjustment of the exercise price and number of shares issuable upon the exercise thereof in the event of certain reclassification of shares, stock dividends or other distributions, capital reorganizations, consolidations, subdivisions, stock splits and combinations;

- have a net exercise provision under which its holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of the Common Stock at the time of exercise of the warrant after deduction of the aggregate exercise price.

Warrants Issued to Avenue

In June 2022, Legacy Orchestra entered into the 2022 Loan and Security Agreement. Pursuant to the terms of the 2022 Loan and Security Agreement, Legacy Orchestra issued two warrants to Avenue on June 3, 2022 that are exercisable for an aggregate of 100,000 shares of Common Stock at an exercise price of $4.06. These warrants (i) terminate on June 3, 2027, (ii) provide for the adjustment of the exercise price and number of shares issuable upon the exercise thereof in the event of certain reclassifications of shares, stock dividends or other distributions, consolidations, subdivisions, stock splits and combinations; and (iii) have a net exercise provision under which its holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of the Common Stock at the time of exercise of the warrant after deduction of the aggregate exercise price.

In connection with the repayment and termination of the 2022 Loan and Security Agreement, we issued two warrants to purchase an aggregate of 27,707 shares of Common Stock at an exercise price of $ 7.67 to Avenue on October 6, 2023 in lieu of a portion of certain fees we owed pursuant to the 2022 Loan and Security Agreement. These warrants (i) terminate on October 6, 2028, (ii) provide for the adjustment of the exercise price and number of shares issuable upon the exercise thereof in the event of certain reclassifications

of shares, stock dividends or other distributions, consolidations, subdivisions, stock splits and combinations; and (iii) have a net exercise provision under which its holders may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of the Common Stock at the time of exercise of the warrant after deduction of the aggregate exercise price.

Piggyback Registration Rights

If Orchestra determines to register for sale any Common Stock under the Securities Act in an underwritten offering, the holders of approximately 1,844,090 shares of Common Stock are entitled to certain "piggyback" registration rights pursuant to the subscription agreements for the Series B-1 Preferred Stock (the "Subscription Agreements"). Pursuant to the "piggyback" registration rights, these holders may require us to include all or a portion of their Common Stock in a registration related to an underwritten offering of our Common Stock, subject to certain limitations. However, the underwriters have the right, subject to specified conditions, to limit the number of shares of Common Stock such holders may include in any underwritten offering.

The Subscription Agreements provide that each party to a Subscription Agreement shall pay its own fees and expenses in connection with the Subscription Agreement and the transactions contemplated thereby.

There is no termination provision with respect to the "piggyback" registration rights contained in the Subscription Agreements.

Amended and Restated Registration Rights and Lock-Up Agreement

In connection with the Business Combination, we entered into the Amended and Restated Registration Rights Agreement with RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Biotech Opportunities Ltd (formerly RTW Venture Fund Limited) (together, the "RTW Funds"), certain former shareholders of HSAC2 and certain former stockholders of Legacy Orchestra with respect to the resale of up to 750,000 HSAC2 Warrants exercisable for Common Stock and up to 21,812,857 Resale Shares of Common Stock (including up to 1,325,000 shares of Common Stock issuable upon exercise of the Warrants). Pursuant to the terms of the Amended and Restated Registration Rights Agreement, we are required to, among other things, file a shelf registration statement to register the Resale Shares and the HSAC2 Warrants on a delayed or continuous basis. Initially, the registration was required to be filed by no later than May 26, 2023. However, the Company and the requisite holders of registrable securities have waived the requirement to file a registration statement until October 23, 2023. In addition, subject to certain limited exceptions, we are required to use our commercially reasonable to cause such registration statement to be declared effective as soon as practicable after the filing thereof. In addition, subject to certain requirements and customary conditions, including with regard to the number of requests that may be made and when, the relevant stockholders may request to sell all or any portion of their registrable securities in an underwritten offering so long as the total offering price is reasonably expected to exceed, in the aggregate, $25 million. The stockholders party to the Amended and Restated Registration Rights Agreement also have certain "piggy-back" registration rights that require us to include such securities in registration statements that we otherwise file, subject to certain requirements and customary conditions. The Amended and Restated Registration Rights Agreement does not contain liquidated damages provisions or other cash settlement provisions resulting from delays in registering the securities. We will bear the expenses incurred in connection with the filing of any such registration statements. The Amended and Restated Registration Rights Agreement contains customary indemnification provisions.

Pursuant to the Amended and Restated Registration Rights Agreement, the signatories thereto agreed, subject to certain customary exceptions, not to (i) sell, assign, offer to sell, contract or agree to sell, grant any option to purchase or otherwise dispose of or agree to dispose of, directly or indirectly, any Lock-up Shares, (ii) establish or increase a put equivalent position or liquidation with respect to or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, with respect to any shares of the Common Stock or any security convertible into or exercisable or exchanged for the Common Stock beneficially owned or owned of record by such signatories (the "Lock-up Shares"), (iii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of any Lock-up Shares, or (iv) publicly announce an intention to effect any of the foregoing during the lock-up period set forth in the Amended and Restated Registration Rights Agreement.

Anti-Takeover Effects of our Governing Documents under Delaware Law

Certain provisions of Delaware law, along with our Charter and our Bylaws, all of which are summarized below, may have the effect of delaying, deferring or discouraging another person from acquiring control of the Company. These provisions are expected to

discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of the Company to first negotiate with our Board. However, these provisions could have the effect of delaying, discouraging or preventing attempts to acquire the Company, which could deprive our stockholders of opportunities to sell their shares of Common Stock at prices higher than prevailing market prices.

Election and Removal of Directors

Our Board consists of seven directors. The exact number of directors will be fixed from time to time by resolution of the Board. No director may be removed except for cause, and directors may be removed for cause by an affirmative vote of shares representing a majority of the shares then entitled to vote at an election of directors. Any vacancy occurring on the Board and any newly created directorship may be filled only by a majority of the remaining directors in office or by the sole remaining director.

Limits on Written Consents

The Charter and the Bylaws provide that holders of Common Stock will not be able to act by written consent without a meeting.

Special Meetings of Stockholders

The Bylaws provide that special meetings of stockholders may be called only by the chairperson of the Board, our chief executive officer or a majority of the directors.

Advance notice requirements for stockholder proposals and director nominations

The Bylaws provide that stockholders seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must provide timely notice of their intent in writing. To be timely, a stockholder's notice will need to be received by the secretary at our principal executive offices not later than the close of business on the 90th day nor earlier than the close of business on the 120th day prior to the first anniversary of the preceding year's annual meeting of stockholders; provided, however, that, in the event that the date of the annual meeting is advanced more than 30 days prior to or delayed by more than 30 days after the anniversary of the preceding year's annual meeting, notice by the stockholder to be timely must be received not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90th day prior to such annual meeting or, if later than the 90th day prior to such annual meeting, the tenth day following the day on which public announcement of the date of such meeting is first made. The Bylaws provide that an adjournment or a postponement of an annual meeting for which notice has been given, or the public announcement thereof has been made, will not commence a new time period (or extend any time period) for the giving of a stockholder's notice as described above. Pursuant to Rule 14a-8 of the Exchange Act, proposals seeking inclusion in the annual proxy statement must comply with the notice periods contained therein. The Bylaws also specify certain requirements as to the form and content of a stockholders' meeting. These provisions may preclude our stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual meeting of stockholders.

Authorized but unissued shares

Our authorized but unissued Common Stock and Preferred Stock will be available for future issuances without stockholder approval and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved Common Stock and Preferred Stock could render more difficult or discourage an attempt to obtain control of the Company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum Selection

The Charter provides that, unless the Company otherwise consents in writing, the Court of Chancery (the "Chancery Court") of the State of Delaware (or, in the event that the Chancery Court does not have subject matter jurisdiction, another state or federal court located within the State of Delaware) will, to the fullest extent permitted by law, be the sole and exclusive forum for resolution of (a) any derivative action or proceeding brought on behalf of the Company, (b) any action, suit or proceeding asserting a claim of breach of a fiduciary duty owed by any director, officer or stockholder of the Company to the Company or to the stockholders of the

Company, (c) any action, suit or proceeding arising pursuant to any provision of the DGCL, the Charter or the Bylaws or (d) any action, suit or proceeding asserting a claim against the Company governed by the internal affairs doctrine. If any action the subject matter of which is described in the immediately preceding sentence is filed in a court other than the courts in the State of Delaware (a "Foreign Action") in the name of any stockholder, such stockholder will be deemed to have consented to (x) the personal jurisdiction of the state and federal courts in the State of Delaware in connection with any action brought in any such court to enforce the provisions of the immediately preceding sentence and (y) having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder.

Notwithstanding the foregoing, unless the Company otherwise consents in writing, the federal district courts of the United States will be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of Common Stock shall be deemed to have notice of and consented to the forum provisions in the Charter.

Notwithstanding the foregoing, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

Limitation of Liability of Directors and Officers

Our Charter provides that we may indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. For information regarding the limitation of liability of our directors and officers, please refer to the section titled "*Management—Limitations on Liability and Indemnification of Directors and Officers*."

Listing

Our shares of Common Stock are currently listed on the Nasdaq Global Market under the symbol "OBIO."

Transfer Agent and Registrar

The transfer agent and registrar for our Common Stock is Continental Stock Transfer & Trust Company, located at 17 Battery Place, New York, New York 10004.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by Paul Hastings LLP, New York, New York.

EXPERTS

The consolidated financial statements of Orchestra BioMed Holdings, Inc. at December 31, 2022 and 2021, and for the years then ended, appearing in this prospectus have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-1, including exhibits, under the Securities Act, with respect to the securities offered by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our securities, you should refer to the registration statement of which this prospectus is a part and the exhibits to such registration statement. The descriptions in this prospectus of the provisions of documents filed as exhibits to this prospectus are only summaries of those documents' material terms. You can read copies of such documents, along with copies of reports, proxy statements and other information filed by us with the SEC at the SEC's website at *http://www.sec.gov*.

We also maintain a website at www.orchestrabiomed.com. Through our website, we make available, free of charge, annual, quarterly and current reports, proxy statements and other information as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained on, or that may be accessed through, our website is not part of, and is not incorporated into, this prospectus and the inclusion of our website address in this prospectus is an inactive textual reference only.

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ORCHESTRA BIOMED HOLDINGS, INC.

Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	June 30, 2023	December 31, 2022
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 16,409	$ 19,784
Marketable securities	101,295	63,915
Strategic investments, current portion	69	86
Accounts receivable, net	171	96
Inventory	178	276
Prepaid expenses and other current assets	1,468	533
Total current assets	119,590	84,690
Property and equipment, net	1,407	1,489
Right-of-use assets	1,874	2,187
Strategic investments, less current portion	2,495	2,495
Deposits and other assets	517	4,711
TOTAL ASSETS	$ 125,883	$ 95,572
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 3,011	$ 3,968
Accrued expenses and other liabilities	3,826	5,376
Operating lease liability, current portion	729	697
Warrant liability	—	2,089
Deferred revenue, current portion	4,294	6,436
Total current liabilities	11,860	18,566
Deferred revenue, less current portion	13,498	13,103
Loan payable	9,563	9,490
Operating lease liability, less current portion	1,310	1,683
Other long-term liabilities	213	196
TOTAL LIABILITIES	36,444	43,038
STOCKHOLDERS' EQUITY		
Preferred stock, $0.0001 par value per share; 10,000,000 shares authorized; none issued or outstanding at June 30, 2023 and December 31, 2022.	—	—
Common stock, $0.0001 par value per share; 340,000,000 shares authorized; 35,743,007 and 20,187,850 shares issued and outstanding as of June 30, 2023 and December 31, 2022, respectively.	4	2
Additional paid-in capital	312,251	252,274
Accumulated other comprehensive loss	(96)	(8)
Accumulated deficit	(222,720)	(199,734)
TOTAL STOCKHOLDERS' EQUITY	89,439	52,534
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 125,883	$ 95,572

The accompanying notes are an integral part of these condensed consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Revenue:				
Partnership revenue	$ 728	$ 229	$ 1,747	$ 945
Product revenue	187	172	332	322
Total revenue	915	401	2,079	1,267
Expenses:				
Cost of product revenues	54	60	98	102
Research and development	8,499	5,029	16,753	8,503
Selling, general and administrative	5,318	2,946	9,729	5,424
Total expenses	13,871	8,035	26,580	14,029
Loss from operations	(12,956)	(7,634)	(24,501)	(12,762)
Other income (expense):				
Interest income (expense), net	941	(246)	1,826	(482)
Loss on fair value adjustment of warrant liability	—	(1,015)	(294)	(1,160)
Loss on debt extinguishment	—	(682)	—	(682)
(Loss) gain on fair value of strategic investments	(31)	1,730	(17)	1,510
Total other income (expense)	910	(213)	1,515	(814)
Net loss	$ (12,046)	$ (7,847)	$ (22,986)	$ (13,576)
Net loss per share				
Basic and diluted	$ (0.35)	$ (0.77)	$ (0.74)	$ (0.74)
Weighted-average shares used in computing net loss per share, basic and diluted	34,613,466	10,138,169	31,228,323	18,446,239
Comprehensive loss				
Net loss	$ (12,046)	$ (7,847)	$ (22,986)	$ (13,576)
Unrealized loss on marketable securities	(61)	—	(88)	—
Comprehensive loss	$ (12,107)	$ (7,847)	$ (23,074)	$ (13,576)

The accompanying notes are an integral part of these condensed consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Condensed Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share and per share data)
(Unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance, January 1, 2023 (as previously reported)	35,694,179	$ 165,923	2,522,214	$ —	$ 86,353	$ (8)	$ (199,734)	$ (113,389)
Retroactive application of reverse capitalization (Note 3)	(35,694,179)	(165,923)	17,665,636	2	165,921	—	—	165,923
Balance, January 1, 2023 effect of Merger	—	—	20,187,850	2	252,274	(8)	(199,734)	52,534
Effect of Merger and recapitalization (refer to Note 3)	—	—	11,422,741	1	54,301	—	—	54,302
Reclassification of Legacy Orchestra common stock warrants to stockholders' equity	—	—	—	—	2,373	—	—	2,373
Unrealized loss on marketable securities	—	—	—	—	—	(27)	—	(27)
Stock-based compensation	—	—	—	—	1,489	—	—	1,489
Exercise of stock options	—	—	2,325	—	10	—	—	10
Exercise of warrants	—	—	128,231	—	11	—	—	11
Net loss	—	—	—	—	—	—	(10,940)	(10,940)
Balance, March 31, 2023	—	$ —	31,741,147	$ 3	$ 310,458	$ (35)	$ (210,674)	$ 99,752
Issuance of shares in settlement of earnout	—	—	3,999,987	1	—	—	—	1
Unrealized loss on marketable securities	—	—	—	—	—	(61)	—	(61)
Stock-based compensation	—	—	—	—	1,707	—	—	1,707
Exercise of stock options	—	—	15,500	—	64	—	—	64
Exercise of warrants	—	—	32,279	—	22	—	—	22
Forfeiture of restricted stock awards	—	—	(45,906)	—	—	—	—	—
Net loss	—	—	—	—	—	—	(12,046)	(12,046)
Balance, June 30, 2023	—	$ —	35,743,007	$ 4	$ 312,251	$ (96)	$ (222,720)	$ 89,439

The accompanying notes are an integral part of these condensed consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Condensed Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share and per share data)
(Unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance, January 1, 2022 (as previously reported)	12,075,976	$ 51,452	2,185,297	$ —	$ 94,894	$ —	$ (166,126)	$ (71,232)
Retroactive application of reverse capitalization (Note 3)	(12,075,976)	(51,452)	6,636,983	1	51,451	—	—	51,452
Balance, January 1, 2022 effect of Merger	—	—	8,822,280	1	146,345	—	(166,126)	(19,780)
Stock-based compensation	—	—	—	—	70	—	—	70
Exercise of stock options	—	—	5,696	—	25	—	—	25
Exercise of warrants	—	—	68,588	—	230	—	—	230
Proceeds from private placement financing	—	—	1,240,169	—	25,262	—	—	25,262
Net loss	—	—	—	—	—	—	(5,729)	(5,729)
Balance, March 31, 2022	—	$ —	10,136,733	$ 1	$ 171,932	$ —	$ (171,855)	$ 78
Stock-based compensation	—	—	—	—	219	—	—	219
Exercise of stock options	—	—	21,442	—	92	—	—	92
Exercise of warrants	—	—	4,650	—	(151)	—	—	(151)
Proceeds from private placement financing	—	—	10,015,015	1	76,392	—	—	76,393
Shares issued pursuant to consulting agreement	—	—	—	—	38	—	—	38
Issuance of warrants pursuant to debt refinancing	—	—	9,300	—	178	—	—	178
Other	—	—	—	—	506	—	—	506
Net loss	—	—	—	—	—	—	(7,847)	(7,847)
Balance, June 30, 2022	—	$ —	20,187,140	$ 2	$ 249,206	$ —	$ (179,702)	$ 69,506

The accompanying notes are an integral part of these condensed consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Condensed Consolidated Statements of Cash Flows
(in thousands, except share and per share data)
(Unaudited)

	Six Months Ended June 30, 2023	Six Months Ended June 30, 2022
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (22,986)	$ (13,576)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	144	98
Shares issued as compensation for consulting services	—	38
Stock-based compensation	3,196	289
Loss on fair value adjustment of warrant liability	294	1,160
Loss (gain) on fair value of strategic investments	17	(1,510)
Accretion and interest related to marketable securities	(2,118)	—
Loss on debt extinguishment	—	682
Non-cash lease expense	313	269
Amortization of deferred financing fees	73	91
Changes in operating assets and liabilities:		
Accounts receivable	(75)	41
Inventory	98	(65)
Prepaid expenses and other assets	(723)	(485)
Accounts payable, accrued expenses and other liabilities	(1,016)	672
Operating lease liabilities – current and non-current	(341)	(48)
Deferred revenue	(1,747)	(945)
Net cash used in operating activities	(24,871)	(13,289)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(62)	(313)
Sales of marketable securities	64,200	—
Purchases of marketable securities	(99,549)	(208)
Net cash used in investing activities	(35,411)	(521)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayment of debt financing, inclusive of debt extinguishment costs	—	(6,446)
Proceeds from Avenue term loan	—	10,000
Proceeds from exercise of warrants	23	79
Proceeds from exercise of stock options	74	117
Effect of merger, net of transaction costs (Note 3)	56,810	—
Proceeds from private placement financing	—	109,830
Deferred financing, offering and merger costs	—	(2,735)
Net cash provided by financing activities	56,907	110,845
Net (decrease) increase in cash and cash equivalents	(3,375)	97,035
Cash and cash equivalents, beginning of the period	19,784	9,938
Cash and cash equivalents, end of the period	$ 16,409	$ 106,973
Supplemental Disclosures of Cash Flow Information		
Cash paid during the six months ended June 30:		
Interest	$ 718	$ 741
Non-cash financing activities:		
Deferred offering and merger costs in accounts payable and accrued expenses	—	6,844
Warrants issued pursuant to private placement financing	—	620
Warrants issued pursuant to debt financing	—	178

The accompanying notes are an integral part of these condensed consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Organization and Basis of Presentation

Orchestra BioMed Holdings, Inc. (formerly known as Health Sciences Acquisitions Corporation 2) (collectively, with its subsidiaries, "Orchestra" or the "Company") is a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. The Company's partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products it develops. The Company's flagship product candidates are BackBeat Cardiac Neuromodulation Therapy ("BackBeat CNT") for the treatment of hypertension ("HTN"), a significant risk factor for death worldwide, and Virtue Sirolimus AngioInfusion Balloon ("Virtue SAB") for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide.

Prior to January 26, 2023, the Company was a special purpose acquisition company formed for the purpose of entering into a merger, amalgamation, share exchange, asset acquisition, share purchase, reorganization or similar business combination with one or more businesses or entities. On January 26, 2023 (the "Closing Date"), the Company consummated the business combination contemplated by the Agreement and Plan of Merger, dated as of July 4, 2022 (as amended by Amendment No. 1 to Agreement and Plan of Merger, dated July 21, 2022, and Amendment No. 2 to Agreement and Plan of Merger, dated November 21, 2022, the "Merger Agreement") by and among Health Sciences Acquisitions Corporation 2, a special purpose acquisition company incorporated as a Cayman Islands exempted company in 2020 ("HSAC2"), HSAC Olympus Merger Sub, Inc., a Delaware corporation and wholly owned subsidiary of HSAC2 ("Merger Sub"), and Orchestra BioMed, Inc. ("Legacy Orchestra"). Pursuant to the Merger Agreement, (i) HSAC2 deregistered in the Cayman Islands in accordance with the Companies Act (2022 Revision) (As Revised) of the Cayman Islands and domesticated as a Delaware corporation in accordance with Section 388 of the Delaware General Corporation Law (the "Domestication") and (ii) Merger Sub merged with and into Legacy Orchestra, with Legacy Orchestra as the surviving company in the merger and, after giving effect to such merger, continuing as a wholly owned subsidiary of Orchestra (the "Merger" and, together with the Domestication and the other transactions contemplated by the Merger Agreement, the "Business Combination"). As part of the Domestication, the Company's name was changed from "Health Sciences Acquisitions Corporation 2" to "Orchestra BioMed Holdings, Inc." See Note 3 for additional information.

Legacy Orchestra, the Company's wholly owned subsidiary, was incorporated in Delaware in January 2017 and was formed to acquire operating and other assets as well as to raise capital conducted through private placements. In May 2018, Legacy Orchestra concurrently completed its formation mergers (the "Formation Mergers") with Caliber Therapeutics, Inc. ("Caliber"), a Delaware corporation, BackBeat Medical, Inc. ("BackBeat"), a Delaware Corporation, and FreeHold Surgical, Inc. ("FreeHold"), a Delaware corporation.

Caliber

Caliber was incorporated in Delaware in October 2005 and began development of its lead product Virtue SAB in 2008. Virtue SAB is a patented drug/device combination product candidate for the treatment of artery disease that delivers a proprietary extended release formulation of sirolimus called SirolimusEFR to the vessel wall during balloon angioplasty without any coating on the balloon surface or the need for leaving a permanent implant such as a stent in the artery. In 2019, Legacy Orchestra entered into a distribution agreement with Terumo Medical Corporation ("Terumo") for global development and commercialization of Virtue SAB (the "Terumo Agreement") (See Note 4).

BackBeat

BackBeat was incorporated in Delaware in January 2010 and began development of its lead product BackBeat CNT that same year. BackBeat CNT is a patented implantable cardiac stimulation-based treatment for hypertension that is designed to immediately, substantially and persistently lower blood pressure while simultaneously modulating autonomic nervous system responses that normally drive and maintain blood pressure higher. BackBeat is currently in a pre-revenue stage of operations. Refer to Note 5 for details regarding the Exclusive License and Collaboration Agreement, dated as of June 30, 2022, by and among, Legacy Orchestra, BackBeat Medical, LLC and Medtronic, Inc. (an affiliate of Medtronic plc) (the “Medtronic Agreement”).

FreeHold

FreeHold was incorporated in Delaware in May 2010 and began development of its hands-free, intracorporeal retractor device for minimally-invasive surgery in 2012. FreeHold is engaged in the development, sales and marketing of its retractor products that provide optimized visual and total surgeon control during laparoscopic and robotic procedures.

Basis of Presentation and Liquidity

The accompanying unaudited interim condensed consolidated financial statements have been prepared pursuant to the rules and regulation of the U.S. Securities and Exchange Commission (“SEC”) for interim financial reporting. These condensed statements are unaudited and, in the opinion of management, include all adjustments (consisting of normal recurring adjustments and accruals) necessary to fairly present the results of the interim periods. The condensed consolidated balance sheet at December 31, 2022 has been derived from the audited financial statements at that date. Operating results and cash flows for the six months ended June 30, 2023 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2023 or any other future period. Certain information and footnote disclosures normally included in annual financial statements prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”) have been omitted in accordance with the rules and regulations for interim reporting of the SEC. These interim condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements included in our report for the year ended December 31, 2022 together with the related notes thereto, filed as Exhibit 99.1 to the Company’s Form 8-K/A filed with the SEC on March 24, 2023.

The Company has a limited operating history and the sales and income potential of its businesses and markets are unproven. As of June 30, 2023, the Company had an accumulated deficit of $222.7 million and has experienced net losses each year since its inception. The Company expects to incur substantial operating losses in future periods and will require additional capital as it seeks to advance its products to commercialization. The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biomedical device industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding, and history of operating losses.

The Company follows the provisions of Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 205-40, *Presentation of Financial Statements — Going Concern*, which requires management to assess the Company’s ability to continue as a going concern within one year after the date the financial statements are issued.

Based on the available balance of cash and cash equivalents and marketable securities as of June 30, 2023, management has concluded that sufficient capital is available to fund its operations and meet cash requirements through the one-year period subsequent to the issuance date of these financial statements. Management may consider plans to raise capital beyond the one-year period subsequent to the issuance date of these financial statements through issuance of equity securities, debt securities, and/or additional development and commercialization partnerships for other products within the Company’s development pipeline. The source, timing and availability of any future financing will depend principally upon market conditions, and, more specifically, on the progress of the Company’s research and development programs.

2. Summary of Significant Accounting Policies

Reverse Recapitalization

The Business Combination is accounted for as a reverse recapitalization in accordance with U.S. GAAP (the “Reverse Recapitalization”). Under this method of accounting, HSAC2 is treated as the “acquired” company and Legacy Orchestra is treated as

the acquirer for financial reporting purposes. Accordingly, for accounting purposes, the Business Combination was treated as the equivalent of Legacy Orchestra issuing stock for the net assets of HSAC2, accompanied by a recapitalization. Accordingly, all historical financial information presented in these consolidated financial statements represent the operations of Legacy Orchestra, and the shares and corresponding capital amounts and losses per share, prior to the Business Combination, have been retroactively restated based on the exchange ratio established in the Merger Agreement (the "Exchange Ratio"). For additional information on the Business Combination and the Exchange Ratio, see Note 3 to these unaudited condensed consolidated financial statements.

Emerging Growth Company and Smaller Reporting Company Status

The Company is an "emerging growth company," as defined in Section 2(a) of the Securities Act of 1933 (the "Securities Act"), as modified by the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act")., As such, it is eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in its periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Further, Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a Securities Act registration statement declared effective or do not have a class of securities registered under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that an emerging growth company can elect to opt out of the extended transition period and comply with the requirements that apply to non-emerging growth companies but any such election to opt out is irrevocable. The Company has elected not to opt out of such extended transition period which means that when a standard is issued or revised and it has different application dates for public or private companies, the Company, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of the Company's condensed consolidated financial statements with another public company which is neither an emerging growth company nor an emerging growth company which has opted out of using the extended transition period difficult or impossible because of the potential differences in accounting standards used.

The Company will remain an emerging growth company until the earliest of (1) the last day of the fiscal year following the fifth anniversary of the closing of the initial public offering of HSAC2, (2) the last day of the fiscal year in which the Company has total annual gross revenue of at least $1.235 billion, (3) the last day of the fiscal year in which the Company is deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of the Company Common Stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year, or (4) the date on which the Company has issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

The Company is also a "smaller reporting company" as defined in the Exchange Act. The Company may continue to be a smaller reporting company even after the Company is no longer an emerging growth company. The Company may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) the market value of the Company's voting and non-voting Common Stock held by non-affiliates is less than $250.0 million measured on the last business day of the Company's second fiscal quarter, or (ii)(a) the Company's annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of the Company's voting and non-voting Common Stock held by non-affiliates is less than $700.0 million measured on the last business day of the Company's second fiscal quarter.

Use of Estimates

The preparation of the condensed consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the condensed consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates. Areas where significant estimates exist include, but are not limited to, the fair value of stock-based compensation, research and development costs incurred, the fair value of the warrant liability, and the estimated costs to complete the combined performance obligation pursuant to the Terumo Agreement (Note 4).

Cash and Cash Equivalents

Cash and cash equivalents are held in banks or in custodial accounts with banks. Cash equivalents are defined as all liquid investments and money market funds with maturity from date of purchase of 90 days or less that are readily convertible into cash.

Marketable Securities

The Company accounts for its marketable securities with remaining maturities of less than one year, or where its intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. These investments represent debt investments in corporate or government securities that are designated as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders' equity as accumulated other comprehensive income (loss). The disclosed fair value related to the Company's investments is based on market prices from a variety of industry standard data providers and generally represent quoted prices for similar assets in active markets or have been derived from observable market data.

Strategic Investments

Management has made investments in affiliated companies and assesses whether the Company exerts significant influence over its strategic investments. The Company considers the nature and magnitude of its investment, any voting and protective rights it holds, any participation in the governance of the other company, and other relevant factors such as the presence of a collaboration or other business relationships. To date, the Company has concluded that it does not have the ability to exercise significant influence over its strategic investments.

The Company's strategic investments consist of equity investments in common stock of a Motus GI Holdings, Inc. ("Motus GI"), a publicly-held company and related party, and preferred shares of Vivasure Medical Limited ("Vivasure"), a privately-held company and related party. The Company classifies strategic investments on its balance sheet as current assets if the assets are available for use for current operations, and the Company does not have a specific plan to hold the investments for a certain duration of time. The shares held of Motus GI represent equity securities with a readily determinable fair value and are required to be measured at fair value at each reporting period using readily determinable pricing available on a securities exchange, in accordance with the provisions of ASU 2016-01, Recognition and Measurement of Financial Assets and Liabilities. Therefore, the Company categorized the investments as current assets. The investments in Vivasure do not have readily determinable fair values and are recorded at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for identical or similar investments of the same issuer. Additionally, as the investments in Vivasure are not readily marketable, the Company categorized the investments as non-current assets. As of June 30, 2023 and December 31, 2022, the carrying value of the investments in Vivasure was $2.5 million.

Fair Value of Financial Instruments

The Company applies ASC 820, *Fair Value Measurement ("ASC 820")*, which establishes a framework for measuring fair value and clarifies the definition of fair value within that framework. ASC 820 defines fair value as an exit price, which is the price that would be received for an asset or paid to transfer a liability in the Company's principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value hierarchy established in ASC 820 generally requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Observable inputs reflect the assumptions that market participants would use in pricing the asset or liability and are developed based on market data obtained from sources independent of the reporting entity. Unobservable inputs reflect the entity's own assumptions based on market data and the entity's judgments about the assumptions that market participants would use in pricing the asset or liability and are to be developed based on the best information available in the circumstances.

The carrying value of the Company's cash and cash equivalents, accounts receivable, prepaid expense, accounts payable and accrued expenses approximate fair value because of the short-term maturity of these financial instruments. In addition, the Company records its investment in Motus GI, marketable securities, and warrant liabilities at fair value. In addition, at June 30, 2023, the Company believed the carrying value of debt approximates fair value as the interest rates were reflective of the rate the Company could obtain on debt with similar terms and conditions. See Note 6 for additional information regarding fair value measurements.

The valuation hierarchy is composed of three levels. The classification within the valuation hierarchy is based on the lowest level of input that is significant to the fair value measurement. The levels within the valuation hierarchy are described below:

Level 1 — Assets and liabilities with unadjusted, quoted prices listed on active market exchanges. Inputs to the fair value measurement are observable inputs, such as quoted prices in active markets for identical assets or liabilities.

Level 2 — Inputs to the fair value measurement are determined using prices for recently traded assets and liabilities with similar underlying terms, as well as direct or indirect observable inputs, such as interest rates and yield curves that are observable at commonly quoted intervals.

Level 3 — Inputs to the fair value measurement are unobservable inputs, such as estimates, assumptions, and valuation techniques when little or no market data exists for the assets or liabilities.

Accounts Receivable and Allowance for Doubtful Accounts

Accounts receivable represent amounts due from customers. The allowance for doubtful accounts is recorded for estimated losses by evaluating various factors, including relative creditworthiness of each customer, historical collections experience and aging of the receivable. As of June 30, 2023 and December 31, 2022, an allowance for doubtful accounts was not deemed necessary.

Inventory

Inventory is stated at the lower of standard cost (which approximates actual cost on a first-in, first-out basis) and net realizable value. Net realizable value represents the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal and transportation. The Company analyzes its inventory levels and writes down inventory that has become obsolete or has a cost basis in excess of its expected net realizable value or inventory quantities in excess of expected requirements. Excess requirements are determined based on comparison of existing inventories to forecasted sales, with consideration given to inventory shelf life. Expired inventory is disposed of, and the related costs are recognized in cost of goods sold. As of June 30, 2023 and December 31, 2022, an impairment charge as a result of obsolete inventory was not deemed necessary.

Research and Development Prepayments, Accruals and Related Expenses

The Company incurs costs of research and development activities conducted by its third-party service providers, which include the conduct of preclinical and clinical studies. The Company is required to estimate its prepaid and accrued research and development costs at each reporting date. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with our service providers. The Company determines the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers, as to the progress or stage of completion of trials or services, as of the end of the reporting period, pursuant to contracts with the third parties and the agreed upon fee to be paid for such services. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are accepted by the Company or the services are performed. Accruals are recorded for the amounts of services provided that have not yet been invoiced.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized over the lesser of their useful life or the remaining life of the lease. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Maintenance and repairs are charged to operations as incurred.

Asset category	Depreciable life
Manufacturing equipment	10 years
Office equipment	3 – 7 years
Research and development equipment	7 years

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the terms of the arrangement. The Company accounts for a contract as a lease when it has the right to control the asset for a period of time while obtaining substantially all of the asset's economic benefits. The Company determines the initial classification and measurement of its operating right-of-use ("ROU") assets and operating lease liabilities at the lease commencement date, and thereafter if modified. The lease term includes any renewal options that the Company is reasonably assured to exercise. The Company's policy is to not record leases with a lease term of 12 months or less on its balance sheets.

The ROU asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, the Company uses its estimated secured incremental borrowing rate for that lease term. Lease expense for operating leases is recognized on a straight-line basis over the reasonably assured lease term based on the total lease payments and is included in operating expense in the statements of operations.

Payments due under each lease agreement include fixed and variable payments. Variable payments relate to the Company's share of the lessor's operating costs associated with the underlying asset and are recognized when the event on which those payments are assessed occurs. Variable payments have been excluded from the lease liability and associated right-of-use asset.

The interest rate implicit in lease agreements is typically not readily determinable, and as such, the Company utilizes the incremental borrowing rate to calculate lease liabilities, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

Debt Discount and Debt Issuance Costs

Debt discounts and debt issuance costs incurred in connection with the issuance of debt are capitalized and reflected as a reduction to the related debt liability. The costs are amortized to interest expense over the term of the debt using the effective-interest method.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. The Company has not identified any such impairment losses to date.

Warrants

The Company evaluates its warrants to determine if the contracts qualify as liabilities in accordance with ASC 480-10, *Distinguishing Liabilities from Equity,* and ASC 815, *Derivatives and Hedging* ("ASC 815"). If the warrant is determined to meet the criteria to be liability classified, the warrant liability is marked-to-market each balance sheet date and recorded as a liability, with the change in fair value recorded in the Company's condensed consolidated statements of operations and comprehensive loss as gain (loss) on fair value adjustment of warrant liability within other income or expense.

In bundled transactions, the proceeds received from any debt instruments and liability classified warrants are allocated to the warrant at fair value first, and the residual value is then allocated to the debt instrument. Upon conversion or exercise of a warrant that is subject to liability treatment, the instrument is marked to fair value at the conversion or exercise date and the fair value is reclassified to equity. Equity classified warrants are recorded within additional paid-in capital at the time of issuance at fair value as of the issuance date and are not subject to subsequent remeasurement.

Revenue Recognition

The Company recognizes revenue under the core principle according to ASC 606, *Revenue from Contracts with Customers ("ASC 606")*, to depict the transfer of control to the Company's customers in an amount reflecting the consideration the Company expects to be entitled to. In order to achieve that core principle, the Company applies the following five step approach: (1) identify the contract with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when a performance obligation is satisfied.

The Company's revenues are currently comprised of product revenue from the sale of FreeHold's intracorporeal organ retractors, and partnership revenues from the Terumo Agreement related to the development and commercialization of Virtue SAB.

Product Revenues

Product revenues related to sales of FreeHold's intracorporeal organ retractors are recognized at a point-in-time upon the shipment of the product to the customer, and there are no significant estimates or judgments related to estimating the transaction price. The product revenues consist of a single performance obligation, and the payment terms are typically 30 days. Product revenues are recognized solely in the United States.

Partnership Revenues

To date, the Company's partnership revenues have related to the Terumo Agreement as further described in Note 4. In future periods, partnership revenues may also include revenues related to the Medtronic Agreement as discussed in Note 5.

The Company assessed whether the Terumo Agreement fell within the scope of ASC 808, *Collaborative Arrangements ("ASC 808")* based on whether the arrangement involved joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. The Company determined that the Terumo Agreement did not fall within the scope of ASC 808. The Company then analyzed the arrangement pursuant to the provisions of ASC 606 and determined that the arrangement represents a contract with a customer and is therefore within the scope of ASC 606.

The promised goods or services in the Terumo Agreement include (i) license rights to the Company's intellectual property, and (ii) research and development services. The Company also has optional additional items in the Terumo Agreement which are considered marketing offers and are accounted for as separate contracts with the customer if such option is elected by the customer, unless the option provides a material right which would not be provided without entering into the contract. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources or (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct in the Terumo Agreement, the Company considered factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

The Company estimates the transaction price for the Terumo Agreement performance obligations based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration includes both fixed consideration and variable consideration. At the inception of the Terumo Agreement, as well as at each reporting period, the Company evaluates the amount of potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected amount method to estimate the amount expected to be received based on which method better predicts the amount expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

The Terumo Agreement contains development and regulatory milestone payments. At contract inception and at each reporting period, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect partnership revenues and earnings in the period of adjustment.

The Terumo Agreement also includes sales-based royalties and the license is deemed to be the predominant item to which the royalties relate. Accordingly, the Company will recognize royalty revenue when the related sales occur. To date, the Company has not recognized any royalty revenue under the arrangement.

The Company has determined that intellectual property licensed to Terumo and the research and development services to be provided through the premarket approval by the U.S. Food and Drug Administration (the “FDA”) for the in-stent restenosis (“ISR”) indication represent a combined performance obligation that is satisfied over time, and that the appropriate method of measuring progress for purposes of recognizing revenues relates to a proportional performance model that measures the proportional performance based on the costs incurred to date relative to the total costs expected to be incurred through the completion of the performance obligation. The Company evaluates the measure of progress at each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company receives payments from Terumo based on billing schedules established in the contract. Such billings for milestone related events have 10-day terms from the date the milestone is achieved, royalty payments are 20-day terms after the close of each quarter, any optional services are 20 days after receipt of an invoice and any sales of the SirolimusEFR are within 30 days after receipt of the shipping invoices. Upfront payments are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the right to consideration is unconditional.

Stock-Based Compensation

The Company applies ASC 718-10, *Compensation — Stock Compensation*, which requires the measurement and recognition of compensation expenses for all stock-based payment awards made to employees and directors including employee stock options under the Company’s stock plans based on estimated fair values (see Note 11). Each award vests over the subsequent period during which the recipient is required to provide service in exchange for the award (the vesting period). The cost of each award is recognized as an expense in the financial statements over the respective vesting period on a straight-line basis.

Under the requirements of ASU 2018-07, the Company accounts for stock-based compensation to nonemployees under the fair value method, which requires all such compensation to be calculated based on the fair value at the measurement date (generally the grant date) and recognized in the Company’s condensed consolidated statements of operations and comprehensive loss over the requisite service period. The Company accounts for forfeitures of stock-based awards as they occur.

Net Loss Per Share

Basic and diluted net loss per share is calculated by dividing net loss by the weighted-average number of shares of common stock outstanding for the period, without consideration of potential dilutive shares of common stock. Since the Company was in a loss position for the periods presented, basic net loss is the same as diluted net loss since the effects of potentially dilutive securities are antidilutive. Potentially dilutive securities include all outstanding warrants, stock options, Earnout Consideration (Note 3) and unvested restricted stock awards. Shares of Company Common Stock outstanding but subject to forfeiture and cancellation by the

Company (e.g., the Forfeitable Shares (as defined in Note 3)) are excluded from the weighted-average number of shares until the period in which such shares are no longer subject to forfeiture. In periods in which there is net income, the Company would apply the two-class method to compute net income per share. Under this method, earnings are allocated to common stock and participating securities based on their respective rights to receive dividends, as if all undistributed earnings for the period were distributed. The two-class method does not apply in periods in which a net loss is reported.

Income Taxes

The Company accounts for income taxes using the asset-and-liability method in accordance with ASC 740, *Income Taxes ("ASC 740")*. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on the deferred tax assets and liabilities of a change in tax rate is recognized in the period that includes the enactment date. A valuation allowance is recorded if it is more-likely-than-not that some portion or all the deferred tax assets will not be realized in future periods. At June 30, 2023 and December 31, 2022, the Company recorded a full valuation allowance on its deferred tax assets.

The Company follows the guidance in ASC Topic 740-10 in assessing uncertain tax positions. The standard applies to all tax positions and clarifies the recognition of tax benefits in the financial statements by providing for a two-step approach of recognition and measurement. The first step involves assessing whether the tax position is more-likely-than-not to be sustained upon examination based upon its technical merits. The second step involves measurement of the amount to be recognized. Tax positions that meet the more-likely than-not threshold are measured at the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate finalization with the taxing authority. The Company recognizes the impact of an uncertain income tax position in the financial statements if it believes that the position is more likely than not to be sustained by the relevant taxing authority. The Company will recognize interest and penalties related to tax positions in income tax expense.

Deferred Offering and Merger Costs

Offering and merger costs, consisting of legal, accounting, printer and filing fees were deferred to be offset against proceeds received when the Business Combination was completed. As of December 31, 2022, there were $4.0 million of deferred transaction costs included in deposits and other assets on the accompanying condensed consolidated balance sheet. Upon the close of the Business Combination, these deferred costs were recorded against net proceeds in additional paid-in capital. For further discussion on the Business Combination, see Note 3.

Defined Contribution Plan

The Company has a defined retirement savings plan under Section 401(k) of the Internal Revenue Code. This plan allows eligible employees to defer a portion of their annual compensation on a pre-tax basis. Effective January 1, 2023, the Company participates in a matching safe harbor 401(k) Plan with a Company contribution of up to 3.5% of each eligible participating employee's compensation. Safe harbor contributions vest immediately for each participant. During the three and six months ended June 30, 2023, the Company made $67,000 and $181,000, respectively, in contributions under this safe harbor 401(k) Plan.

Comprehensive Loss

Comprehensive loss is comprised of net loss and changes in unrealized gains and losses on the Company's available-for-sale investments.

Segment Reporting

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company has determined it operates in one segment.

New Accounting Standards

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. During 2018 and 2019, the FASB also issued subsequent amendments to the initial guidance (collectively, "Topic 326"). Topic 326 requires organizations to measure all expected credit losses for financial instruments held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. The Company adopted ASU 2016-13 as of January 1, 2023. The adoption of ASU 2016-13 did not have a material impact on the Company's condensed consolidated financial statements.

3. Business Combination and Recapitalization

On January 26, 2023, Legacy Orchestra and HSAC2 consummated the Business Combination, with Legacy Orchestra surviving as a wholly owned subsidiary of HSAC2. As part of the Business Combination, HSAC2 changed its name to Orchestra BioMed Holdings, Inc. Upon the closing of the Business Combination (the "Closing"), the Company's certificate of incorporation provided for, among other things, a total number of authorized shares of capital stock of 350,000,000 shares, of which 340,000,000 shares were designated common stock, $0.0001 par value per share, and of which 10,000,000 shares were designated preferred stock, $0.0001 par value per share.

The Business Combination is accounted for as a reverse recapitalization in accordance with U.S. GAAP. Under this method of accounting, HSAC2 is treated as the "acquired" company and Legacy Orchestra is treated as the acquirer for financial reporting purposes. Accordingly, for accounting purposes, the Business Combination was treated as the equivalent of Legacy Orchestra issuing stock for the net assets of HSAC2, accompanied by a recapitalization. The net assets of HSAC2 are stated at historical cost, with no goodwill or intangible assets recorded.

In connection with the Business Combination, HSAC 2 Holdings, LLC (the "Sponsor") agreed that 25% or 1,000,000 shares of its shares of common stock of the Company ("Company Common Stock") will be forfeited to the Company (the "Forfeitable Shares") on the first business day following the fifth anniversary of the Closing unless, as to 500,000 shares, the volume-weighted average price of the Company Common Stock is greater than or equal to $15.00 per share over any 20 trading days within any 30-trading day period (the "Initial Milestone Event"), and as to the remaining 500,000 shares, the volume-weighted average price of the Company Common Stock is greater than or equal to $20.00 per share over any 20 trading days within any 30-trading day period (the "Final Milestone Event"). Further, the Sponsor and HSAC2's other initial shareholders prior to HSAC2's initial public offering (the "HSAC2 IPO") agreed to subject (i) the 4,000,000 shares of Company Common Stock issued to HSAC2's initial shareholders prior to the HSAC2 IPO (the "Insider Shares") and (ii) the 450,000 shares of Company Common Stock purchased in a private placement simultaneously with the HSAC2 IPO (the "Private Shares") to a lock-up for up to 12 months following the Closing, and the Sponsor forfeited 50% of its 1,500,000 warrants in HSAC2 purchased upon consummation of the HSAC2 IPO (the "Private Warrants"), comprising 750,000 Private Warrants, for no consideration, immediately prior to the Closing (the "Sponsor Forfeiture"). Pursuant to the terms of the Merger Agreement, immediately following the Sponsor Forfeiture and prior to the Closing, HSAC2 issued 750,000 warrants to purchase Company Common Stock to eleven specified employees and directors of Legacy Orchestra. These new warrants have substantially similar terms to the forfeited Private Warrants, except that they will become exercisable between 24 and 36 months after the Closing. On April 12, 2023, the Initial Milestone Event was achieved, and, as a result, 500,000 of the Forfeitable Shares are no longer subject to forfeiture.

In connection with the Business Combination, existing Legacy Orchestra stockholders also had the opportunity to elect to participate in an earnout (the "Earnout") pursuant to which each such electing stockholder (an "Earnout Participant") may receive a portion of additional contingent consideration of up to 8,000,000 shares of Company Common Stock in the aggregate ("Earnout Consideration"). Each Earnout Participant agreed to extend their applicable lock-up period from 6 months to 12 months, pursuant to an Earnout Election Agreement and such Earnout Participants will collectively be entitled to receive: (i) 4,000,000 shares of the Earnout Consideration, in the aggregate, in the event that, from the time beginning immediately after the Closing until the fifth anniversary of the Closing Date (the "Earnout Period"), the Initial Milestone Event occurs; and (ii) an additional 4,000,000 shares of the Earnout Consideration, in the aggregate, in the event that, during the Earnout Period, the Final Milestone Event occurs. Approximately, 91% of Legacy Orchestra stockholders elected to participate in the Earnout. On April 12, 2023, the Initial Milestone Event was achieved, and each Earnout Participant was issued their Pro Rata Portion (as such term is defined in the Merger Agreement) of 4,000,000 shares of Company Common Stock, resulting in a total of 3,999,987 shares of Company Common Stock being issued due to rounding.

Simultaneously with the execution of the Merger Agreement, HSAC2 and Legacy Orchestra entered into separate forward purchase agreements (each, as amended, a "Forward Purchase Agreement" and, together, the "Forward Purchase Agreements") with certain funds managed by RTW Investments, LP (the "RTW Funds") and Covidien Group S.à.r.l., an affiliate of Medtronic plc ("Medtronic" and the RTW Funds, each a "Purchasing Party"), pursuant to which each of the Purchasing Parties agreed to purchase $10 million of ordinary shares of HSAC2 ("HSAC2 Ordinary Shares") immediately prior to the Domestication (as defined below), less the dollar amount of HSAC2 Ordinary Shares holding redemption rights that the Purchasing Party acquired and held until immediately prior to the Domestication (such HSAC2 Ordinary Shares either purchased from HSAC2 or acquired and held until immediately prior to the Domestication, the "Forward Purchase Shares"). The RTW Funds completed their purchases of HSAC2 Ordinary Shares under their Forward Purchase Agreement on or before July 22, 2022. Medtronic completed approximately $9.9 million of purchases of HSAC2 Ordinary Shares under its Forward Purchase Agreement on or before January 20, 2023. Medtronic subsequently completed $0.1 million in purchases of HSAC2 Ordinary Shares and/or Company Common Stock on or before January 30, 2023.

Simultaneously with the execution of the Merger Agreement and Forward Purchase Agreements, HSAC2, Legacy Orchestra and the RTW Funds entered into a Backstop Agreement (the "Backstop Agreement"), pursuant to which the RTW Funds, jointly and severally, agreed to purchase such number of HSAC2 Ordinary Shares at a price of $10.00 per share to the extent that the amount of cash remaining in HSAC2's working capital and trust account as of immediately prior to the closing of the Merger was less than $60 million (which calculation excludes amounts received pursuant to Medtronic's Forward Purchase Agreement or are otherwise held in HSAC2's trust account established pursuant to the HSAC2 IPO (the "HSAC2 Trust Account") in respect of Medtronic's Forward Purchase Shares, but is inclusive of amounts received pursuant to the RTW Funds' Forward Purchase Agreement and otherwise held in the HSAC2 Trust Account in respect of the RTW Funds' Forward Purchase Shares). Pursuant to the Backstop Agreement, the RTW Funds purchased 1,808,512 HSAC2 Ordinary Shares on January 25, 2023, immediately prior to the Domestication.

Immediately prior to the closing of the Business Combination, each issued and outstanding share of Legacy Orchestra preferred stock (the "Legacy Orchestra Preferred Stock") was canceled and converted into shares of Legacy Orchestra common stock (the "Legacy Orchestra Common Stock") based on predetermined ratios (see Note 9).

Upon the consummation of the Business Combination, each issued and outstanding share of Legacy Orchestra Common Stock was canceled and converted into the right to receive shares of Company Common Stock based upon the Exchange Ratio. The shares and corresponding capital amounts and loss per share related to Legacy Orchestra Common Stock prior to the Business Combination have been retroactively restated to reflect the Exchange Ratio.

Outstanding stock options, whether vested or unvested, to purchase shares of Legacy Orchestra Common Stock ("Legacy Orchestra Options") granted under the Orchestra BioMed, Inc. 2018 Stock Incentive Plan ("2018 Plan") (see Note 11) converted into stock options for shares of Company Common Stock upon the same terms and conditions that were in effect with respect to such stock options immediately prior to the Business Combination, after giving effect to the Exchange Ratio (the "Exchanged Options").

The following table details the number of shares of Company Common Stock issued immediately following the consummation of the Business Combination:

	Number of Shares
Common stock of HSAC2, outstanding prior to the Business Combination	6,762,117
Less: Redemption of HSAC2 shares	(1,597,888)
Common stock held by former HSAC2 shareholders	5,164,229
HSAC2 sponsor shares	4,450,000
Shares issued related to Backstop Agreement	1,808,512
Total shares outstanding prior to issuance of merger consideration to Legacy Orchestra stockholders	11,422,741
Shares issued to Legacy Orchestra stockholders – Company Common Stock[1]	20,191,338
Total shares of Company Common Stock immediately after Business Combination[2]	31,614,079

(1) The number of shares of common stock issued to Legacy Orchestra equity holders was determined based on (i) 2,522,214 shares of Legacy Orchestra Common Stock outstanding immediately prior to the closing of the Business Combination converted based on the Exchange Ratio and

(ii) 35,694,179 shares of Legacy Orchestra Preferred Stock outstanding immediately prior to the closing of the Business Combination converted based on the Exchange Ratio. All fractional shares were rounded down.

(2) Excludes 8,000,000 shares of Company Common Stock issued or to be issued based on satisfaction of the Initial Milestone Event and the Final Milestone Event. On April 12, 2023, the Initial Milestone Event was achieved, and each Earnout Participant was issued their Pro Rata Portion (as such term is defined in the Merger Agreement) of 4,000,000 shares of Company Common Stock, resulting in a total of 3,999,987 shares of Company Common Stock being issued due to rounding.

The following table reconciles the elements of the Business Combination to the Company's condensed consolidated statement of changes in stockholders' equity (deficit) (in thousands):

	Amount
Cash – HSAC2's trust (net of redemption)	$ 51,915
Cash – Backstop Agreement	18,085
Gross proceeds	70,000
Less: HSAC2 and Legacy Orchestra transaction costs paid	(15,698)
Effect of Business Combination, net of redemptions and transaction costs	$ 54,302

The $54.3 million above differs from the $56.8 million effect of the Business Combination on the condensed consolidated statements of cash flows, due to $2.5 million of transaction costs paid by Legacy Orchestra in 2022.

4. Terumo Agreement

In June 2019, Legacy Orchestra entered into the Terumo Agreement, pursuant to which Terumo secured global commercialization rights for Virtue SAB in coronary and peripheral vascular indications (the "Terumo Indications"). Under this agreement, Legacy Orchestra received an upfront payment of $30 million and an equity commitment of up to $5 million of which $2.5 million was invested in June 2019 as part of the Legacy Orchestra Series B-1 financing and $2.5 million was invested in June 2022 as part of the Legacy Orchestra Series D-2 financing. The Company was initially eligible to receive up to $65 million in additional payments based on the achievement of certain development and regulatory milestones and is also eligible to earn royalties on future sales by Terumo based on royalty rates ranging from 10 – 15%. Of these milestone payments, $35 million relate to achieving certain milestones by specified target achievement dates. As of the issuance date of these financial statements, the target achievement date for two $5 million milestone payments has already passed. In addition, due to delays in the Company's Virtue SAB program resulting from the COVID-19 pandemic, supply chain issues and unexpected changes to regulatory requirements, including increased testing and other activities related to chemistry, manufacturing, and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, the Company is unlikely to be able to complete the remaining time-based milestones by the specified target achievement dates to earn the remaining $25 million in time-based milestone payments pursuant to the Terumo Agreement. Although the Company is currently negotiating with Terumo mutually agreeable adjustments to certain target achievement dates to reflect the regulatory and pandemic-related delays, there is no assurance as to the outcome of these negotiations with respect to any potential modifications to the milestone target achievement dates. Pursuant to the terms of the Terumo Agreement, Legacy Orchestra licensed intellectual property rights to Terumo and the Company is primarily responsible for completing the development of the product in the United States through premarket approval by the FDA for the ISR indication. These research and development services to be provided by the Company include (i) manufacturing, testing and packaging the drug required for the clinical trials, (ii) supplying Terumo with information related to the design and manufacture of the delivery device and the technology transfer needed for Terumo to ultimately commence manufacture of the delivery device, and (iii) carrying out regulatory activities related to clinical trials in the United States for the ISR indication.

The Company has concluded that the license granted to Terumo is not distinct from the research and development services that will be provided to Terumo through the completion of the development of ISR indication, as Terumo cannot obtain the benefit of the license without the related research and development services. Accordingly, the Company will recognize revenues for this combined performance obligation over the estimated period of research and development services using a proportional performance model. The Company measures proportional performance based on the costs incurred relative to the total estimated costs of the research and development services.

In 2019, Legacy Orchestra received a total of $32.5 million from Terumo related to the stock purchase and the revenue generating elements of the Terumo Agreement. The Company recorded the estimated fair value of the shares of $2.5 million in stockholders' equity, as the value paid by Terumo is consistent with the value paid by other third-party stockholders in Legacy Orchestra's offering of its Series B-1 Preferred Stock. The Company allocated the remaining $30 million to the transaction price of the Terumo Agreement. The Company considers the future potential development and regulatory milestones to be variable consideration, which are fully constrained from the transaction price as of June 30, 2023 and December 31, 2022, as the achievement of such milestone payments are uncertain and highly susceptible to factors outside of the Company's control. The Company plans to re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur. In addition, the arrangement also includes sales-based royalties on product sales by Terumo subsequent to commercialization ranging from 10 - 15%, none of which have been recognized to date.

The Company recorded the $30 million upfront payment received from Terumo in 2019 within deferred revenue. The following table presents the changes in the Company's deferred revenue balance from the Terumo Agreement during the three and six months ended June 30, 2023 and 2022:

Deferred Revenue – December 31, 2022 (in thousands)	$	19,539
Revenue recognized		(1,747)
Deferred Revenue – June 30, 2023	$	17,792
Deferred Revenue – December 31, 2021	$	22,401
Revenue recognized		(945)
Deferred Revenue – June 30, 2022	$	21,456

The Company's balance of deferred revenue contains the transaction price from the Terumo Agreement allocated to the combined license and research and development performance obligation, which was partially unsatisfied as of June 30, 2023. The Company expects to recognize approximately $4.3 million of its deferred revenue during the next twelve months and recognize the remaining approximately $13.5 million through the remainder of the performance period, which is currently estimated to be completed in 2026 - 2027 and may be impacted by the actual clinical and regulatory timelines of the program.

As of each quarterly reporting date, the Company evaluates its estimates of the total costs expected to be incurred through the completion of the combined performance obligation and updates its estimates as necessary. For the three months ended June 30, 2023 and 2022, the expenses incurred related to the Terumo Agreement were approximately $4.5 million and $3.9 million, respectively. For the six months ended June 30, 2023 and 2022, the expenses incurred related to the Terumo Agreement were approximately $8.3 million and $6.6 million, respectively. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 3% as of June 30, 2023, as compared to the estimates as of December 31, 2022, and increased by approximately 10% as of June 30, 2022, as compared to the estimates as of December 31, 2021. While the Company believes it has estimated total costs associated with the Terumo Agreement through completion, these estimates encompass a broad range of expenses over a multi-year period and, as such, are subject to periodic changes as new information becomes available. The impact of the changes in estimates resulted in a reduction of partnership revenues of $392,000 and $836,000 for the three months ended June 30, 2023 and 2022, respectively, as compared to the amounts that would have been recorded based on the previous estimates. The impact of the changes in estimates resulted in a reduction of partnership revenues of $303,000 and $847,000 for the six months ended June 30, 2023 and 2022, respectively, as compared to the amounts that would have been recorded based on the previous estimates. The impact of these changes in estimates on the net loss per share attributable to common stockholders, basic and diluted, for the three months ended June 30, 2023 and 2022 was an increase of $0.01 and $0.08. The impact of these changes in estimates on the net loss per share attributable to common stockholders, basic and diluted, for the six months ended June 30, 2023 and 2022 was an increase of $0.01 and $0.05.

The Company will also manufacture, or have manufactured, SirolimusEFR and has exclusive rights to sell it on a per unit basis to Terumo for use in the Virtue SAB product. The Company has determined that this promise does not contain a material right as the pricing is based on standalone selling prices. Through June 30, 2023, there have been no additional amounts recognized as revenue under the Terumo Agreement other than the recognition of a portion of the upfront payment described above.

5. Medtronic Agreement

In June 2022, Legacy Orchestra, BackBeat Medical, LLC and Medtronic entered into the Medtronic Agreement for the development and commercialization of BackBeat CNT for the treatment of hypertension (“HTN”) in patients indicated for a cardiac pacemaker (the “Primary Field”). Under the terms of the Medtronic Agreement, the Company will sponsor a multinational pivotal study to support regulatory approval of BackBeat CNT in the Primary Field and be financially responsible for development, clinical and regulatory costs associated with this pivotal study. Medtronic is currently working with the Company to integrate BackBeat CNT into its top-of-the-line, commercially available dual-chamber pacemaker system for use in the pivotal trial and will provide development, clinical and regulatory resources in support of the pivotal trial, for which the Company will reimburse Medtronic at cost.

Under the terms of the Medtronic Agreement, Medtronic will have exclusive rights to commercialize BackBeat CNT-enabled pacing systems globally following receipt of regulatory approval. Medtronic would be entirely responsible for global commercialization following receipt of regulatory approvals, including manufacturing, sales, marketing and distribution costs.

The Company is expected to receive between $500 and $1,600 per BackBeat CNT-enabled device sold based on a formula of the higher of (1) a fixed dollar amount per BackBeat CNT-enabled device (amount varies materially on a country-by-country basis) or (2) a percentage of the BackBeat CNT-generated sales. Procedures using the BackBeat CNT-enabled pacemakers are expected to be billed under existing reimbursement codes.

Medtronic has a right of first negotiation through FDA approval of BackBeat CNT in the Primary Field, to expand its global rights to BackBeat CNT for the treatment of HTN patients not indicated for a pacemaker.

The Company assessed whether the Medtronic Agreement fell within the scope of ASC 808 and concluded that the Medtronic Agreement is a collaboration within the scope of ASC 808. In addition, the Company determined that Medtronic is a customer for a good or service that is a distinct unit of account, and therefore, the transactions in the Medtronic Agreement should be accounted for under ASC 606.

The Company has concluded that the license granted to Medtronic is not distinct from the development and implementation services that will be provided to Medtronic through the completion of the development of HTN indication, as Medtronic cannot obtain the benefit of the license without the related development and implementation services. ASC 606-10-55-65 includes an exception for the recognition of revenue relating to licenses of intellectual property with sales-based or usage-based royalties. Under this exception, royalty revenue is not recorded until the subsequent sale or usage occurs, or the performance obligation has been satisfied, whichever is later.

The Company concluded that the exemption applies and therefore, the royalty revenue associated with these performance obligations will be recognized as the underlying sales occur. Additionally, pursuant to the Medtronic Agreement, expenses incurred by Medtronic in connection with clinical device development and regulatory activities performed will be reimbursed by the Company. The Company will record such expenses as research and development expenses as incurred. During the three and six months ended June 30, 2023, the Company incurred approximately $1.0 million and $2.3 million, respectively, of research and development costs related to these reimbursements to the Medtronic Agreement, of which $1.9 million is included within accounts payable and accrued expenses in the Company’s June 30, 2023 condensed consolidated balance sheet.

Concurrently with the close of the Medtronic Agreement, Legacy Orchestra also received a $40 million investment from Medtronic in connection with Legacy Orchestra’s Series D-2 Preferred Stock financing. The equity was purchased at a fair value consistent with the price paid by other investors at that time, and accordingly, the proceeds received were recorded as an equity investment.

Through June 30, 2023, there have been no amounts recognized as revenue under the Medtronic Agreement.

6. Financial Instruments and Fair Value Measurements

The following tables summarize the Company's financial assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy:

(in thousands)	June 30, 2023			
	Level 1	Level 2	Level 3	Total
Assets				
Money market fund (included in cash and cash equivalents)	$ 13,193	$ —	$ —	$ 13,193
Investment in Motus GI (see Note 7)	69	—	—	69
Marketable securities (Corporate and Government debt securities)	—	101,295	—	101,295
Total assets	$ 13,262	$ 101,295	$ —	$ 114,557

(in thousands)	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets				
Money market fund (included in cash and cash equivalents)	$ 8,708	$ —	$ —	$ 8,708
Investment in Motus GI (see Note 7)	86	—	—	86
Marketable securities (Corporate and Government debt securities)	—	63,915	—	63,915
Total assets	$ 8,794	$ 63,915	$ —	$ 72,709
Liabilities:				
Warrant liability (see Note 10)	$ —	$ —	$ 2,089	$ 2,089
Total liabilities	$ —	$ —	$ 2,089	$ 2,089

The Level 2 assets consist of government and corporate debt securities which are valued using market observable inputs, including the current interest rate and other characteristics for similar types of investments, whose fair value may not represent actual transactions of identical securities. There were no transfers between Levels 1, 2 or 3 for the periods presented.

Prior to the closing of the Business Combination, the Company's warrant liability was measured at fair value on a recurring basis using unobservable inputs and were classified as Level 3 inputs, and any change in fair value was recognized as change in fair value of warrant liability in the Company's condensed consolidated statements of operations and comprehensive loss. As of the Closing Date, all Legacy Orchestra liability classified warrants were reclassified to equity. Refer to Note 9 for the valuation technique and assumptions used in estimating the fair value of the warrants and discussion on the change in classification.

The following table presents a roll-forward of the aggregate fair values of the Company's liabilities for which fair value is determined by Level 3 inputs (in thousands):

	Warrant Liability
Balance—December 31, 2022	$ 2,089
Warrants exercised prior to the Business Combination	(10)
Change in fair value of warrants	294
Warrants reclassified to equity	(2,373)
Balance—March 31, 2023	—
Balance—June 30, 2023	$ —

7. Marketable Securities and Strategic Investments

Marketable Securities

The following is a summary of the Company's marketable securities as of June 30, 2023 and December 31, 2022:

	June 30, 2023			
(in thousands)	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 48,100	$ —	$ (39)	$ 48,061
Government debt securities	53,291	—	(57)	53,234
Total	$ 101,391	$ —	$ (96)	$ 101,295

	December 31, 2022			
(in thousands)	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 52,242	$ 7	$ —	$ 52,249
Government debt securities	11,681	—	(15)	11,666
Total	$ 63,923	$ 7	$ (15)	$ 63,915

The Company believes it is more likely than not that its marketable securities in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. To date, the Company has not recorded any allowance for credit losses on its investment securities. The Company determined that the unrealized losses were not attributed to credit risk but were primarily driven by the broader change in interest rates.

For the three and six months ended June 30, 2023, the Company recognized realized losses on its marketable securities of $102,000. For the three and six months ended June 30, 2022, the Company did not recognize any realized gains or losses on its marketable securities.

Strategic Investments

The Company values the Motus GI investment by measuring fair value using the listed share price on the Nasdaq Capital Market on each valuation date.

Aggregate losses of $31,000 and $160,000 during the three months ended June 30, 2023 and 2022, respectively, and aggregate losses of $17,000 and $380,000 during the six months ended June 30, 2023 and 2022, respectively, were recorded to adjust the strategic investments in equity securities of Motus GI to its fair value of $69,000 at June 30, 2023 and $86,000 at December 31, 2022, which is classified as strategic investments within current assets on the accompanying condensed consolidated balance sheets.

The Company's long term strategic investments as of June 30, 2023 represent investments made in Vivasure in 2020, 2021 and 2022 that were originally recorded at cost. There were no observable price changes, other than as described below, or impairments identified during the three and six months ended June 30, 2023 or the three and six months ended June 30, 2022 related to these investments.

In May 2022, Vivasure announced a Series D private placement, in which it received a material investment from Haemonetics Corporation, a new strategic investor. In conjunction with a €30 million investment in Vivasure, Haemonetics Corporation also secured an option to acquire Vivasure based on the achievement of certain milestones. As a result, Legacy Orchestra's existing convertible redeemable notes converted into Series D Preferred Stock of Vivasure in May 2022. The investment in the Vivasure Series D Preferred Stock represents an observable price change in an orderly transaction for an identical instrument of the same issuer, and accordingly, the Company recognized a gain on its strategic investment in Vivasure of $1.9 million in the second quarter of 2022. This amount represents a portion of the previously impaired investment balance described below.

During the fourth quarter of 2019, the Company identified indicators of impairment of Vivasure strategic investments held at that time as a result of adverse changes in Vivasure's business operations, including liquidity concerns. As a result, the Company recorded

an impairment charge in the fourth quarter of 2019 of $5.8 million, which represents the cumulative impairment charges recorded on Vivasure strategic investments to date.

8. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following:

(in thousands)	June 30, 2023	December 31, 2022
Equipment	$ 1,745	$ 1,712
Office furniture	364	364
Leasehold improvements	197	191
Construction in progress	22	—
Property and equipment, gross	2,328	2,267
Less accumulated depreciation and amortization	(921)	(778)
Total Property and equipment, net	$ 1,407	$ 1,489

Depreciation and amortization expense was $72,000 and $49,000 for the three months ended June 30, 2023 and 2022, respectively. Depreciation and amortization expense was $144,000 and $98,000 for the six months ended June 30, 2023 and 2022, respectively.

Accrued Expenses

Accrued expenses consist of the following:

(in thousands)	June 30, 2023	December 31, 2022
Accrued compensation	$ 1,954	$ 2,480
Clinical trial accruals	895	1,003
Other accrued expenses	977	1,893
Total accrued expenses	$ 3,826	$ 5,376

9. Common and Preferred Stock

Common Stock

The Company is authorized to issue up to 340,000,000 shares of Company Common Stock, par value $0.0001 per share.

As discussed in Note 3, the Company has retroactively adjusted the shares issued and outstanding prior to January 26, 2023 to give effect to the Exchange Ratio to determine the number of shares of Company Common Stock into which they were converted.

Preferred Stock

The Company is authorized to issue 10,000,000 shares of preferred stock with a par value of $0.0001 per share. The board of directors of the Company (the "Board") has the authority to issue preferred stock and to determine the rights, privileges, preferences, restrictions, and voting rights of those shares. As of June 30, 2023, no shares of preferred stock were outstanding.

10. Warrants

The Company evaluates its outstanding warrants to determine if the instruments qualify for equity or liability classification.

Private Warrants

Prior to the Merger, HSAC2 had outstanding 1,500,000 Private Warrants, which were issued in connection with the HSAC2 IPO to the Sponsor. Each Private Warrant entitles the holder thereof to purchase one share of Company Common Stock at a price of $11.50 per share, subject to adjustment as provided herein. The Private Warrants became exercisable 30 days after the completion of the Business Combination and will expire five years after the completion of the Business Combination. Each Private Warrant is non-redeemable and may be exercised on a cashless basis. Since these warrants are indexed to the Company's publicly traded common stock, they are classified within equity.

As described in Note 3, the Sponsor and HSAC2's other initial shareholders prior to the HSAC2 IPO agreed to subject (i) the 4,000,000 Insider Shares and (ii) the 450,000 Private Shares to a lock-up for up to 12 months following the Closing and the Sponsor forfeited 50% of its 1,500,000 Private Warrants, comprising 750,000 Private Warrants, for no consideration, immediately prior to the Closing. Pursuant to the terms of the Merger Agreement, immediately following the Sponsor Forfeiture and prior to the Closing, HSAC2 issued 750,000 warrants to purchase Company Common Stock to eleven specified employees and directors of Legacy Orchestra. These new warrants have substantially similar terms to the forfeited Private Warrants, except that they will become exercisable between 24 and 36 months after the Closing.

Assumed Legacy Orchestra Warrants

Prior to the close of the Business Combination, the majority of Legacy Orchestra's warrants (the "Legacy Orchestra Warrants") were required to be accounted for as liabilities as certain features within the warrant agreements contained features that were not considered "fixed for fixed" pursuant to ASC 815, and therefore, the fair value of the warrant liability was marked-to-market at each balance sheet date, with the change in fair value recorded in the Company's condensed consolidated statements of operations and comprehensive loss within other income (expense). Upon the close of the Business Combination, all liability classified Legacy Orchestra Warrants became equity classified on that date, as the warrant agreements became "fixed for fixed." As a result, the warrant liability was fair valued and adjusted from $2.1 million as of December 31, 2022 to $2.4 million as of January 26, 2023, and then subsequently reclassified into stockholders' equity. In addition, Legacy Orchestra also had outstanding other equity classified warrants recorded within additional paid-in capital at the time of issuance at fair value that were not subject to subsequent remeasurement.

The Company calculates the fair value of the outstanding warrant liability at each reporting date by estimating the equity value of the Company, and then utilizing option pricing models to allocate the total equity value to the shares and warrants outstanding. The inputs used in the valuation models for the Company's warrant liability are as follows:

	Period from January 1, 2023 to January 26, 2023	June 30, 2022
Expected volatility	44 – 49%	45 – 54%
Risk-free interest rate	3.60 – 4.80%	2.60 – 3.00%
Remaining term in years	0.35 – 5.00	0.92 – 5.38
Exercise price of common warrants	$1.08 – $30.11	$1.08 – $30.11
Exercise price of Legacy preferred warrants	—	—
Common stock price	$10.63	$9.18
Legacy preferred stock price	—	—
Expected dividend yield	0%	0%

The Company's warrant liability related to Legacy Orchestra warrant activity rollforward is as follows, with the warrants having been converted to reflect the effect of the Merger:

(in thousands, except share data)	Preferred Warrants	Common Warrants	Amount
Balance December 31, 2022	—	1,327,074	$ 2,089
Warrants exercised prior to the business combination	—	(1,163)	(10)
Change in fair value of warrants as of January 26, 2023	—	—	294
Warrants reclassified to equity	—	(1,325,911)	(2,373)
Balance March 31, 2023	—	—	—
Balance June 30, 2023	—	—	$ —

(in thousands, except share data)	Preferred Warrants	Common Warrants	Amount
Balance December 31, 2021	206,997	1,189,162	$ 635
Exercise of warrants	—	(68,587)	(156)
Change in the fair value of warrants	—	—	145
Balance March 31, 2022	206,997	1,120,575	624
Exercise of warrants	—	(4,650)	(15)
Forfeiture of warrants	—	(4,650)	(38)
Issuance of warrants related to Legacy Orchestra preferred stock financing	—	159,965	620
Amendments of existing warrants	(206,997)	206,997	810
Other	—	(150,000)	(335)
Change in the fair value of warrants	—	—	243
Balance June 30, 2022	—	1,328,237	$ 1,909

Private Warrants and Assumed Legacy Orchestra Warrants

The following table summarizes outstanding warrants to purchase shares of Company Common Stock as of June 30, 2023 and December 31, 2022:

	Number of Shares			
	June 30, 2023	December 31, 2022	Exercise Price	Term
Liability-classified Warrants				
Legacy Orchestra Warrants	—	1,327,074	$0.50 – $14.00	0.10 – 4.75
Equity-classified Warrants				
Legacy Orchestra Warrants	541,808	250,000	$0.50 – $14.00	0.10 – 9.00
Private Warrants Held by Sponsor	750,000	1,500,000	$11.50	4.57 – 4.82
Private Warrants Held by Employees (Note 11)	675,000	—	$11.50	4.57
	1,966,808	1,750,000		
Total Outstanding	1,966,808	3,077,074		

11. Stock-Based Compensation

As of June 30, 2023, the only equity compensation plan from which the Company may currently issue new awards is the Company's 2023 Equity Incentive Plan (the "2023 Plan"), as more fully described below.

Orchestra BioMed, Inc. 2018 Stock Incentive Plan

Prior to the Merger, Legacy Orchestra maintained the 2018 Plan, under which Legacy Orchestra granted incentive stock options, non-qualified stock options and restricted stock awards to its employees and certain non-employees, including consultants, advisors and directors. The maximum aggregate shares of Legacy Orchestra Common Stock that was subject to awards and issuable under the 2018 Plan was 5.2 million shares prior to the Merger. Employees, consultants, and directors were eligible for awards granted

under the 2018 Plan which generally have a contractual life of up to 10 years and may be exercisable in cash or as otherwise determined by the Board. Vesting generally occurs over a period of not greater than three years.

As described in Note 3, in connection with the Merger, each Legacy Orchestra Option that was outstanding and unexercised immediately prior to the time that the Merger became effective (the “Effective Time”) (whether vested or unvested) was assumed by the Company and converted into an option to purchase an adjusted number of shares of Company Common Stock at an adjusted exercise price per share, based on the Exchange Ratio, and will continue to be governed by substantially the same terms and conditions, including vesting, as were applicable to the former option. Each Exchanged Option is exercisable for a number of whole shares of Company Common Stock equal to the product of the number of shares of Legacy Orchestra Common Stock underlying such Legacy Orchestra Options multiplied by the Exchange Ratio, and the per share exercise price of such Exchanged Option is equal to the quotient determined by dividing the exercise price per share of the Legacy Orchestra Option by the Exchange Ratio. Following the closing of the Merger, no new awards may be made under the 2018 Plan.

The Company accounted for the Exchanged Options as a modification of the existing options. Incremental compensation costs, measured as the excess, if any, of the fair value of the modified options over the fair value of the original options immediately before its terms are modified, is measured based on the fair value of the underlying shares and other pertinent factors at the modification date. The impact of the option modifications were de minimis.

Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan

At the Effective Time, the Company adopted the 2023 Plan which permits the granting of incentive stock options, non-qualified options, stock appreciation rights, restricted stock, restricted stock units, performance awards and other stock-based award to employees, directors, and non-employee consultants and/or advisors. As of June 30, 2023, 3,561,678 shares of Company Common Stock are authorized for issuance pursuant to awards under the 2023 Plan. The pool of available shares will be automatically increased on the first day of each calendar year, beginning January 1, 2023 and ending January 1, 2032, by an amount equal to the lesser of (i) 4.8% of the outstanding shares of our Common Stock determined on a fully-diluted basis as of the immediately preceding December 31 and (ii) 3,036,722 shares of Common Stock, and (iii) such number of shares of Common Stock determined by the Board or the Compensation Committee prior to January 1st of a given year.

In addition, any awards outstanding under the 2018 Plan upon the Closing, after adjustment for the Business Combination, remain outstanding. If any of those awards subsequently expire, terminate, or are surrendered or forfeited for any reason without issuance of shares after the closing of the Business Combination, the shares of Company Common Stock underlying those awards will automatically become available for issuance under the 2023 Plan.

Total stock-based compensation related to option issuances was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(in thousands)	**2023**	**2022**	**2023**	**2022**
Research and development	$ 330	$ 52	$ 815	$ 91
Selling, general and administrative	631	91	1,369	107
Total stock-based compensation	$ 961	$ 143	$ 2,184	$ 198

As of June 30, 2023, there was approximately $6.6 million of unrecognized stock-based compensation expense associated with the stock options noted above that is expected to be recognized over a weighted average period of three years.

Total stock-based compensation related to restricted stock was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(in thousands)	**2023**	**2022**	**2023**	**2022**
Research and development	$ —	$ —	$ —	$ —
Selling, general and administrative	498	76	547	91
Total stock-based compensation	$ 498	$ 76	$ 547	$ 91

As of June 30, 2023, there was approximately $312,000 of unrecognized restricted stock-based compensation expense associated with the restricted stock noted above that is expected to be recognized over a weighted average period of approximately three years.

As previously discussed in Note 3 and Note 10, pursuant to the terms of the Merger Agreement, immediately following the Sponsor Forfeiture and prior to the Closing, the Company issued 750,000 warrants to purchase Company Common Stock to eleven specified employees and directors of Legacy Orchestra. These warrants have substantially similar terms to the forfeited Private Warrants, except that they will become exercisable between 24 and 36 months after the Business Combination. The estimated grant-date fair value of these warrant awards issued concurrent with the close of the Business Combination was calculated using the Black-Scholes option pricing model. Assumptions used were an expected term (in years) of 5.00, expected volatility of 50%, risk-free interest rate of 3.54%, expected dividend yield of 0%, and fair value of common stock of $10.63. During the three and six months ended June 30, 2023, 75,000 of these warrants were forfeited resulting in a remaining 675,000 warrants outstanding.

Total stock-based compensation related to warrants was as follows:

(in thousands)	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Research and development	$ 120	$ —	$ 207	$ —
Selling, general and administrative	128	—	258	—
Total stock-based compensation	$ 248	$ —	$ 465	$ —

As of June 30, 2023, there was approximately $2.8 million of unrecognized stock-based compensation expense associated with the warrants noted above that is expected to be recognized over a weighted average period of approximately three years.

Stock Option Activity

The following table summarizes the stock option activity of the Company under the 2018 Plan and the 2023 Plan:

	Shares Underlying Options	Weighted Average Exercise Price	Weighted Average Remaining Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2023	7,868,448	3.51	8.35	—
Retroactive application of Reverse Recapitalization (Note 3)	(4,209,620)	4.05	—	—
Outstanding at January 1, 2023, effect of Merger	3,658,828	7.56	8.35	—
Granted	323,175	9.89	—	—
Exercised	(17,825)	4.16	—	—
Forfeited/canceled	(142,256)	5.35	—	—
Outstanding June 30, 2023	3,821,922	7.97	5.31	$ 4,002
Exercisable at June 30, 2023	2,163,768	6.60	7.09	$ 3,412

The following table summarizes the restricted stock activity of the Company under the Plan:

	Restricted Stock Outstanding	Weighted Average Remaining Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding January 1, 2023	158,589	9.14	—
Granted	—	—	—
Vested	(63,451)	—	—
Forfeited/canceled	(45,901)	—	—
Outstanding June 30, 2023	49,237	8.67	$ 549

During the six months ended June 30, 2023, the Company did not grant any restricted stock awards (“RSAs”) while 63,451 RSAs vested at a weighted-average grant date fair value of $3.52.

Determination of Stock Option Awards Fair Value

The estimated grant-date fair value of all the Company's option awards was calculated using the Black-Scholes option pricing model, based on the following weighted average assumptions:

	Six Months Ended June 30,	
	2023	2022
Expected term (in years)	6.00	6.00
Expected volatility	50 %	49 %
Risk-free interest rate	3.60 %	2.70 %
Expected dividend yield	0 %	0 %
Fair value of common stock	$ 9.63	$ 4.06

The fair value of each stock option grant was determined by the Company using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

Expected Term — The expected term represents the period that stock-based awards are expected to be outstanding. The Company's historical share option exercise information is limited due to a lack of sufficient data points and did not provide a reasonable basis upon which to estimate an expected term. The expected term for option grants is therefore determined using the "simplified" method, as prescribed in the Securities and Exchange Commission's Staff Accounting Bulletin (SAB) No. 107. The simplified method deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards.

Expected Volatility — The expected volatility was derived from the historical stock volatilities of comparable peer public companies within the Company's industry that are considered to be comparable to the Company's business over a period equivalent to the expected term of the stock-based awards since there has been no trading history of the Legacy Orchestra Common Stock and limited trading history of the Company.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the stock-based awards' expected term.

Expected Dividend Yield — The expected dividend yield is zero as neither the Company nor Legacy Orchestra has paid, and the Company does not anticipate paying, any dividends on its common stock in the foreseeable future.

Fair Value of Common Stock — Prior to the Business Combination, as the Legacy Orchestra Common Stock has not historically been publicly traded, its board of directors periodically estimated the fair value of the Company's common stock considering, among other things, contemporaneous valuations of its common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Subsequent to the Business Combination, the Company utilizes the price of its publicly-traded Company Common Stock to determine the grant date fair value of awards.

12. Leases

Office Lease

In August 2019, Legacy Orchestra entered into an addendum to the original December 2009 lease agreement for 8,052 square feet of office space in New Hope, PA. The lease will expire in September 2024. Monthly fees will be between $9,000 and $19,000 for the period from commencement through termination.

In November 2019, Legacy Orchestra entered into a new lease agreement for approximately 5,200 square feet of office space in New York, NY. The lease will expire in March 2028. Monthly fees will be between $28,000 and $30,000 for the period from commencement through termination.

In January 2020, Legacy Orchestra entered into an agreement for the use of portions of the office space of Motus GI, a related party, in Fort Lauderdale, Florida. The agreement will expire in September 2024. The monthly fee commenced on the month following the date of agreement. Monthly fees will be between $12,000 and $17,000 for the period from commencement through termination.

In May 2022, Legacy Orchestra amended the agreement with Motus GI for a larger portion of the office space and extended the expiration date to November 2024. Monthly fees will be between $7,000 and $23,000 for the period from commencement of the amendment to expiration. The amount paid is estimated to be proportionate to the percentage of space used by the Company applied to the monthly rent obligated to be paid by Motus GI to their landlord.

Operating cash flow supplemental information for the six months ended June 30, 2023:

Cash paid for amounts included in the present value of operating lease liabilities was $410,000 during the six months ended June 30, 2023 compared to $354,000 during the six months ended June 30, 2022.

As of June 30, 2023:	
Weighted average remaining lease term – operating leases, in years	3.73
Weighted average discount rate – operating leases	6.25 %

Operating Leases

Rent/lease expense for office and lab space was approximately $209,000 and $180,000 for the three months ended June 30, 2023 and 2022, respectively. Rent/lease expense for office and lab space was approximately $417,000 and $354,000 for the six months ended June 30, 2023 and 2022, respectively. The table below shows the future minimum rental payments, exclusive of taxes, insurance, and other costs, under the leases as of June 30, 2023:

Year ending December 31:	Operating Leases (in thousands)
2023 (remaining six months)	$ 413
2024	727
2025	352
2026	352
2027	352
Thereafter	88
Total future minimum lease payments	$ 2,284
Imputed interest	(245)
Total liability	$ 2,039

13. Related Party Transactions

In addition to transactions and balances related to cash and stock-based compensation to officers and directors, the Company had the following transactions and balances with related parties during the year ended 2022 and the six months ended June 30, 2023:

Vivasure Investments

In December 2020 and 2021, and April 2022, Legacy Orchestra invested in Vivasure, a related party, $183,000, $213,000, and $208,000, respectively, in the form of unsecured convertible redeemable notes. The unsecured convertible redeemable notes converted into Series D preferred stock of Vivasure in May of 2022 (Note 7).

14. Debt Financing

In June 2022, Legacy Orchestra entered into a loan and security agreement (the “2022 Loan and Security Agreement”) with Avenue Venture Opportunities Fund, L.P. (“Avenue I”) and Avenue Venture Opportunities Fund II, L.P. (“Avenue II,” and,

collectively with Avenue I, “Avenue”). The terms of the 2022 Loan and Security Agreement include a term loan of up to $20 million available in two tranches with the first tranche of $10 million that was drawn at closing in June of 2022, and a second tranche of $10 million available at closing of the Legacy Orchestra Series D-2 Preferred Stock financing was not drawn. Additionally, the Company may have access to a third tranche of $30 million subject to certain financing milestones. The term loan matures on June 1, 2026. In addition, the lender has the right, at its discretion, but not the obligation, to convert any portion of the outstanding principal amount of the loans up to $5 million into shares of Company Common Stock at a price per share equal to $12.00 (the “Conversion Option”), subject to adjustment; provided, however, the Conversion Option shall not be exercised by lender during the six (6) month period after completion of the Business Combination.

Pursuant to the terms of the 2022 Loan and Security Agreement, Legacy Orchestra issued Avenue warrants that will be exercisable for 100,000 shares of Company Common Stock, and the estimated fair value of the warrants of $178,000 was recorded as debt discount on the date of issuance and is being amortized to interest expense over the term of the 2022 Loan and Security Agreement. In addition, other financing costs totaling $405,000 were also recorded as debt discount and is being amortized to interest expense over the term of the facility.

The term loan accrues interest at a floating per annum rate equal to the Wall Street Journal prime rate plus 6.45%. The rate in effect at June 30, 2023 was 14.7%. The repayment terms of the loan include monthly payments over a 4-year period, consisting of an initial 2-year interest-only period, followed by 24 monthly principal payments of $417,000 plus interest. In addition, there is a final payment equal to 4.25% of the initial commitment amount of $20 million, which will be accrued over the term of the loan using the effective-interest method.

Concurrent with the closing of the 2022 Loan and Security Agreement, Legacy Orchestra terminated and repaid an existing 2019 Loan and Security Agreement with Silicon Valley Bank (the “2019 Loan and Security Agreement”), which resulted in a loss on extinguishment of $682,000. Pursuant to the terms of the 2019 Loan and Security Agreement, Legacy Orchestra issued Silicon Valley Bank a warrant that, to the extent Legacy Orchestra made draws on the 2019 Loan and Security Agreement, was exercisable for a number of shares of Legacy Orchestra Common Stock equal to 2% of the amount drawn divided by the exercise price of $1.33 per share of Legacy Orchestra Common Stock. As a result of the draw in December of 2020, Legacy Orchestra issued 150,000 Legacy Orchestra Common Stock warrants to Silicon Valley Bank, and the estimated fair value of the warrants of $544,000 was recorded as debt discount on the date of issuance and was being amortized to interest expense over the term of the credit facility. These warrants have been exercised and are no longer outstanding.

The term loan accrued interest at a floating per annum rate equal to the greater of (i) the Wall Street Journal prime rate plus 1.00% or (ii) 6.25%. In addition, there was a final payment equal to 8.25% of the original aggregate principal amount which accrued over the term of the loan using the effective-interest method.

Total interest expense recorded on these facilities during the three months ended June 30, 2023 and June 30, 2022 was approximately $457,000 and $257,000, respectively. Total interest expense recorded on these facilities during the six months ended June 30, 2023 and June 30, 2022 was approximately $897,000 and $493,000, respectively.

The following table shows the amount of principal payments due pursuant to the term loan by year:

Period ending June 30:	**Principal Payments (in thousands)**
2023 (remaining 6 months)	$ —
2024	2,500
2025	5,000
2026	2,500
Total	$ 10,000

The term loan is secured by all of the Company’s assets, excluding intellectual property and certain other assets. The loan contains customary affirmative and restrictive covenants, including the Company’s ability to enter into fundamental transactions, incur additional indebtedness, grant liens, pay any dividend or make any distributions to its holders, make investments, merge or consolidate with any other person or engage in transactions with the Company’s affiliates, but does not include any financial covenants.

15. Net Loss Per Share

Basic net loss per share of Company Common Stock is computed by dividing net loss by the weighted-average number of shares of Company Common Stock. Shares of Company Common Stock outstanding but subject to forfeiture and cancellation by the Company (e.g., the Forfeitable Shares – see Note 3) are excluded from the weighted-average number of shares until the period in which such shares are no longer subject to forfeiture.

As discussed in Note 3, in connection with the Business Combination, existing Legacy Orchestra stockholders had the opportunity to elect to participate in the Earnout pursuant to which each such Earnout Participant may receive a portion of additional contingent consideration of up to 8,000,000 shares of Earnout Consideration. On April 12, 2023, the Initial Milestone Event was achieved, and each Earnout Participant was issued their Pro Rata Portion (as such term is defined in the Merger Agreement) of 4,000,000 shares of Company Common Stock, resulting in a total of 3,999,987 shares of Company Common Stock being issued due to rounding. Additionally, 500,000 of the Forfeitable Shares are no longer subject to forfeiture as a result of the Initial Milestone Event.

Diluted net loss per share of Company Common Stock includes the effect, if any, from the potential exercise or conversion of securities, such as stock options, Legacy Orchestra Warrants and Private Warrants, and Forfeitable Shares and Earnout Consideration, which would result in the issuance of incremental shares of Company Common Stock, unless their effect would be anti-dilutive.

The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per share for the three and six months ended June 30, 2023 and June 30, 2022, as their effect is anti-dilutive:

	Three and Six Months Ended June 30,	
	2023	2022
Stock options	3,821,922	1,578,316
Company common stock warrants	1,966,808	1,328,237
Unvested restricted stock awards	49,237	168,108
Conversion option	416,667	—
Forfeitable shares	500,000	—
Earnout consideration	4,000,000	—
Total	10,754,634	3,074,661

16. Subsequent Events

On August 8, 2023, the Company announced that the FDA granted investigational device exemption approval with conditions to initiate the Company's planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with Coronary ISR. The Company is permitted to begin enrollment of the study upon completion of standard clinical trial initiation activities including clinical center Institutional Review Board approvals. The conditional approval also requires the Company to submit additional information to the FDA.

On September 19, 2023, the Company announced that the FDA granted investigational device exemption approval to initiate the Company's planned BACKBEAT pivotal study evaluating the efficacy and safety for the development and commercialization of BackBeat CNT, also known as Atrioventricular Interval Modulation (AVIM) therapy for hypertensive pacemaker patients. The Company is permitted to begin enrollment upon completion of standard clinical trial initiation activities, including clinical center Institutional Review Board approvals. The Company expects to begin enrollment in the BACKBEAT pivotal study before the end of 2023.

On October 6, 2023, the Company repaid and terminated the 2022 Loan and Security Agreement. In connection with the repayment and termination, the Company repaid $10 million of principal and issued warrants to purchase 27,707 shares of Company Common Stock at an exercise price of $7.67 per share in lieu of a cash payment of approximately $212,500 due with respect to certain fees under the 2022 Loan and Security Agreement. The Company also paid approximately $849,000 of net interest, prepayment fees, and legal fees.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Orchestra BioMed Holdings, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Orchestra BioMed Holdings, Inc. (the Company) as of December 31, 2021 and 2022 the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2022, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.

Philadelphia, Pennsylvania

March 24, 2023, except for the Business Combination Transaction paragraphs in Note 1, and the last three paragraphs of Note 14, as to which the date is October 10, 2023.

ORCHESTRA BIOMED HOLDINGS, INC.

Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2021	2022
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 9,938	$ 19,784
Marketable securities	—	63,915
Strategic investments, current portion	958	86
Accounts receivable, net	121	96
Inventory	68	276
Prepaid expenses and other current assets	234	533
Total current assets	11,319	84,690
Property and equipment, net	1,120	1,489
Right-of-use assets	—	2,187
Strategic investments, less current portion	398	2,495
Deposits and other assets	690	4,711
TOTAL ASSETS	$ 13,527	$ 95,572
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Accounts payable	$ 2,029	$ 3,968
Accrued expenses and other liabilities	2,034	5,376
Operating lease liability, current portion	—	697
Warrant liability	635	2,089
Deferred revenue, current portion	5,542	6,436
Loan payable, current portion	2,000	—
Total current liabilities	12,240	18,566
Deferred revenue, less current portion	16,859	13,103
Loan payable, less current portion	3,673	9,490
Operating lease liability, less current portion	—	1,683
Other long-term liabilities	535	196
TOTAL LIABILITIES	33,307	43,038
STOCKHOLDERS' EQUITY (DEFICIT)		
Preferred stock, $0.0001 par value per share; 10,000,000 shares authorized; none issued or outstanding at December 31, 2021 and December 31, 2022	—	—
Common stock, $0.0001 par value; 340,000,000 shares authorized; 8,822,280 and 20,187,850 shares issued and outstanding as of December 31, 2021 and December 31, 2022, respectively	1	2
Additional paid-in capital	146,345	252,274
Accumulated other comprehensive loss	—	(8)
Accumulated deficit	(166,126)	(199,734)
TOTAL STOCKHOLDERS' EQUITY (DEFICIT)	(19,780)	52,534
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)	$ 13,527	$ 95,572

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Years Ended December 31,	
	2021	2022
Revenue:		
Partnership revenue	$ (1,475)	$ 2,862
Product revenue	693	671
Total revenue	(782)	3,533
Expenses:		
Cost of product revenues	199	211
Research and development	12,890	21,945
Selling, general and administrative	7,928	14,034
Total expenses	21,017	36,190
Loss from operations	(21,799)	(32,657)
Other income (expense):		
Interest (expense) income, net	(927)	50
Gain (loss) on fair value adjustment of warrant liability	699	(1,350)
Loss on debt extinguishment	—	(682)
(Loss) gain on fair value of strategic investments	(987)	1,031
Total other expense	(1,215)	(951)
Net loss	$ (23,014)	$ (33,608)
Net loss per share		
Basic and diluted	$ (2.61)	$ (2.24)
Weighted-average shares used in computing net loss per share, basic and diluted	8,818,115	14,988,584
Comprehensive loss		
Net loss	$ (23,014)	$ (33,608)
Unrealized gain (loss) on marketable securities	2	(8)
Comprehensive loss	$ (23,012)	$ (33,616)

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share and per share data)
(Unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance, January 1, 2021 (as previously reported)	12,075,976	$ 51,452	2,056,497	$ —	$ 94,572	$ (2)	$ (143,112)	$ (48,542)
Retroactive application of reverse capitalization	(12,075,976)	(51,452)	6,761,598	1	51,451	—	—	51,452
Balance, January 1, 2021 effect of Merger	—	—	8,818,095	1	146,023	(2)	(143,112)	2,910
Unrealized gain on marketable securities	—	—	—	—	—	2	—	2
Stock-based compensation	—	—	—	—	302	—	—	302
Exercise of stock options	—	—	697	—	3	—	—	3
Exercise of warrants	—	—	3,488	—	17	—	—	17
Net loss	—	—	—	—	—	—	(23,014)	(23,014)
Balance, December 31, 2021	—	$ —	8,822,280	$ 1	$ 146,345	$ —	$ (166,126)	$ (19,780)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance, January 1, 2022 (as previously reported)	12,075,976	$ 51,452	2,185,297	$ —	$ 94,894	$ —	$ (166,126)	$ (71,232)
Retroactive application of reverse capitalization	(12,075,976)	(51,452)	6,636,983	1	51,451	—	—	51,452
Balance, January 1, 2022 effect of Merger	—	—	8,822,280	1	146,345	—	(166,126)	(19,780)
Unrealized loss on marketable securities	—	—	—	—	—	(8)	—	(8)
Stock-based compensation	—	—	—	—	3,375	—	—	3,375
Exercise of stock options	—	—	27,848	—	121	—	—	121
Exercise of warrants	—	—	73,238	—	79	—	—	79
Proceeds from private placement financing	—	—	11,255,184	1	101,632	—	—	101,633
Shares issued pursuant to consulting agreement	—	—	9,300	—	38	—	—	38
Issuance of warrants pursuant to debt refinancing	—	—	—	—	178	—	—	178
Other	—	—	—	—	506	—	—	506
Net loss	—	—	—	—	—	—	(33,608)	(33,608)
Balance, December 31, 2022	—	$ —	20,187,850	$ 2	$ 252,274	$ (8)	$ (199,734)	$ 52,534

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

Consolidated Statements of Cash Flows
(in thousands, except share and per share data)

	Years Ended December 31,	
	2021	2022
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (23,014)	$ (33,608)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	181	222
Shares issued as compensation for consulting services	—	38
Stock-based compensation	302	3,375
Deferred rent	(33)	—
(Gain) loss on fair value adjustment of warrant liability	(699)	1,350
Loss (gain) on fair value of strategic investments	987	(1,031)
Loss on debt extinguishment	—	682
Non-cash lease expense	—	571
Accretion and interest related to marketable securities	—	(600)
Amortization of deferred financing fees	217	163
Changes in operating assets and liabilities:		
Accounts receivable	47	25
Inventory	1	(208)
Prepaid expenses and other assets	29	(439)
Accounts payable, accrued expenses and other liabilities	1,078	3,352
Operating lease liabilities – current and non-current	—	(319)
Deferred revenue	1,475	(2,862)
Net cash used in operating activities	(19,429)	(29,289)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(274)	(591)
Purchases of related party convertible notes	(213)	—
Purchases of marketable securities	—	(63,323)
Sales of marketable securities	13,504	—
Purchases of strategic investments	—	(208)
Net cash provided by (used in) investing activities	13,017	(64,122)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayment of debt financing, inclusive of debt extinguishment costs	(4,000)	(6,446)
Proceeds from Avenue term loan	—	10,000
Proceeds from exercise of warrants	4	79
Warrant repurchases	—	(10)
Proceeds from exercise of stock options	3	121
Proceeds from private placement financing	—	109,830
Deferred financing, offering and merger costs	—	(10,317)
Net cash (used in) provided by financing activities	(3,993)	103,257
Net (decrease) increase in cash and cash equivalents	(10,405)	9,846
Cash and cash equivalents, beginning of the period	20,343	9,938
Cash and cash equivalents, end of the period	$ 9,938	$ 19,784
Supplemental Disclosures of Cash Flow Information		
Cash paid during the year for:		
Interest	$ 389	$ 1,371
Non-cash financing activities:		
Deferred offering and merger costs in accounts payable and accrued expenses	100	1,646
Warrants issued pursuant to private placement financing	—	620
Warrants issued pursuant to debt financing	—	178

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Orchestra BioMed Holdings, Inc. (formerly known as Health Sciences Acquisitions Corporation 2) (collectively, with its subsidiaries, "Orchestra" or the "Company") is a biomedical innovation company seeking to provide high-impact solutions for large unmet needs in procedure-based medicine. The Company's partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products it develops. The Company's business model seeks to adapt the strategic partnering tactics widely used by the biopharmaceutical industry to the medical device market. The Company's goal is to accelerate and improve the likelihood of the Company's product candidates reaching patients and providers worldwide by sharing the risks and rewards of developing and commercializing these product candidates with established companies. The Company's flagship product candidates are Virtue Sirolimus AngioInfusion Balloon ("Virtue SAB") for the treatment of artery disease, the leading cause of mortality worldwide, and BackBeat Cardiac Neuromodulation Therapy ("BackBeat CNT") for the treatment of hypertension, a significant risk factor for death worldwide. The Company has additional product candidates in its pipeline and plans to thoughtfully expand its product pipeline in the future through acquisitions, strategic collaborations, licensing and organic development.

Orchestra BioMed, Inc. ("Legacy Orchestra") was incorporated in Delaware in January 2017 and was formed to acquire operating and other assets as well as to raise capital conducted through private placements. In May 2018, Legacy Orchestra concurrently completed its formation mergers (the "Formation Mergers") with Caliber Therapeutics, Inc. ("Caliber"), a Delaware corporation, BackBeat Medical, Inc. ("BackBeat"), a Delaware Corporation, and FreeHold Surgical, Inc. ("FreeHold"), a Delaware corporation.

Caliber

Caliber was incorporated in Delaware in October 2005 and began development of its lead product Virtue SAB in 2008. Virtue SAB is a patented drug/device combination product candidate for the treatment of artery disease that delivers a proprietary extended release formulation of sirolimus called SirolimusEFR to the vessel wall during balloon angioplasty without any coating on the balloon surface or the need for leaving a permanent implant such as a stent in the artery. In 2019, the Company entered into a distribution agreement with Terumo Medical Corporation ("Terumo") for global development and commercialization of Virtue SAB (the "Terumo Agreement") (Note 3).

BackBeat

BackBeat was incorporated in Delaware in January 2010 and began development of its lead product BackBeat CNT that same year. BackBeat CNT is a patented implantable cardiac stimulation-based treatment for hypertension that is designed to immediately, substantially and persistently lower blood pressure while simultaneously modulating autonomic nervous system responses that normally drive and maintain blood pressure higher. BackBeat is currently in a pre-revenue stage of operations. Refer to Note 4 for details regarding the Exclusive License and Collaboration Agreement, dated as of June 30, 2022, by and among, Orchestra, BackBeat Medical, LLC and Medtronic, Inc. (an affiliate of Medtronic plc) (the "Medtronic Agreement").

FreeHold

FreeHold was incorporated in Delaware in May 2010 and began development of its hands-free, intracorporeal retractor device for minimally-invasive surgery in 2012. FreeHold is engaged in the development, sales and marketing of its retractor products that provide optimized visual and total surgeon control during laparoscopic and robotic procedures. The Company generated revenue of approximately $693,000 and $671,000 during the years ended December 31, 2021 and 2022, respectively related to this legacy FreeHold Surgical, Inc. technology.

Business Combination Transaction

Prior to January 26, 2023, Health Sciences Acquisitions Corporation 2 was a special purpose acquisition company formed for the purpose of entering into a merger, amalgamation, share exchange, asset acquisition, share purchase, reorganization or similar business

combination with one or more businesses or entities. On January 26, 2023 (the “Closing Date”), the Company consummated the business combination contemplated by the Agreement and Plan of Merger, dated as of July 4, 2022 (as amended by Amendment No. 1 to Agreement and Plan of Merger, dated July 21, 2022, and Amendment No. 2 to Agreement and Plan of Merger, dated November 21, 2022, the “Merger Agreement”) by and among Health Sciences Acquisitions Corporation 2, a special purpose acquisition company incorporated as a Cayman Islands exempted company in 2020 (“HSAC2”), HSAC Olympus Merger Sub, Inc., a Delaware corporation and wholly owned subsidiary of HSAC2 (“Merger Sub”), and Legacy Orchestra. Pursuant to the Merger Agreement, (i) HSAC2 deregistered in the Cayman Islands in accordance with the Companies Act (2022 Revision) (As Revised) of the Cayman Islands and domesticated as a Delaware corporation in accordance with Section 388 of the Delaware General Corporation Law (the “Domestication”) and (ii) Merger Sub merged with and into Legacy Orchestra, with Legacy Orchestra as the surviving company in the merger and, after giving effect to such merger, continuing as a wholly owned subsidiary of Orchestra (the “Merger” and, together with the Domestication and the other transactions contemplated by the Merger Agreement, the “Business Combination”). As part of the Domestication, the Company’s name was changed from “Health Sciences Acquisitions Corporation 2” to “Orchestra BioMed Holdings, Inc.”

The Business Combination is accounted for as a reverse recapitalization in accordance with U.S. GAAP (the “Reverse Recapitalization”). Under this method of accounting, HSAC2 is treated as the “acquired” company and Legacy Orchestra is treated as the acquirer for financial reporting purposes. Accordingly, for accounting purposes, the Business Combination was treated as the equivalent of Legacy Orchestra issuing stock for the net assets of HSAC2, accompanied by a recapitalization. Accordingly, all historical financial information presented in these consolidated financial statements represent the operations of Legacy Orchestra, and the shares and corresponding capital amounts and losses per share, prior to the Business Combination, have been retroactively restated based on the exchange ratio established in the Merger Agreement (the “Exchange Ratio”). Upon the closing of the Business Combination, the Company’s certificate of incorporation provided for, among other things, a total number of authorized shares of capital stock of 350,000,000 shares, of which 340,000,000 shares were designated common stock, $0.0001 per value per share, and of which 10,000,000 shares were designated preferred stock, $0.0001 par value per share.

Basis of Presentation and Liquidity

The accompanying consolidated financial statements herein have been prepared by the Company in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”).

The Company has a limited operating history and the sales and income potential of its businesses and markets are unproven. As of December 31, 2022, the Company had an accumulated deficit of $199.7 million and has experienced net losses each year since its inception. The Company expects to incur substantial operating losses in future periods and will require additional capital as it seeks to advance its products to commercialization. The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding, and history of operating losses.

The Company follows the provisions of Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 205-40, *Presentation of Financial Statements — Going Concern*, which requires management to assess the Company’s ability to continue as a going concern within one year after the date the financial statements are issued.

Based on the available balance of cash and cash equivalents and marketable securities as of December 31, 2022, as well as the proceeds received from the consummation of the Business Combination in January 2023 (Note 14), management has concluded that sufficient capital is available to fund its operations and meet cash requirements through the one-year period subsequent to the issuance date of these financial statements. Management may consider plans to raise capital beyond the one-year period subsequent to the issuance date of these financial statements through issuance of equity securities, debt securities, and/or additional development and commercialization partnerships for other products within the Company’s development pipeline. The source, timing and availability of any future financing will depend principally upon market conditions, and, more specifically, on the progress of the Company’s research and development programs.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates. Areas where significant estimates exist include, but are not limited to, the fair value of stock-based compensation, research and development costs incurred, the fair value of the warrant liability, and the estimated costs to complete the combined performance obligation pursuant to the Terumo Agreement (Note 3).

Cash and Cash Equivalents

Cash and cash equivalents are held in banks or in custodial accounts with banks. Cash equivalents are defined as all liquid investments and money market funds with maturity from date of purchase of 90 days or less that are readily convertible into cash.

Marketable Securities

The Company accounts for its marketable securities with remaining maturities of less than one year, or where its intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. These investments represent debt investments in corporate or government securities that are designated as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders' deficit as accumulated other comprehensive income (loss). The disclosed fair value related to the Company's investments is based on market prices from a variety of industry standard data providers and generally represent quoted prices for similar assets in active markets or have been derived from observable market data.

Strategic Investments

Management has made investments in affiliated companies and assesses whether the Company exerts significant influence over its strategic investments. The Company considers the nature and magnitude of its investment, any voting and protective rights it holds, any participation in the governance of the other company, and other relevant factors such as the presence of a collaboration or other business relationships. To date, the Company has concluded that it does not have the ability to exercise significant influence over its strategic investments.

The Company's strategic investments consist of equity investments in common stock of a publicly-held company and related party (Motus GI) and preferred shares and convertible notes of a privately-held company and related party (Vivasure). The Company classifies strategic investments on its balance sheet as current assets if the assets are available for use for current operations, and the Company does not have a specific plan to hold the investments for a certain duration of time. The shares held of Motus GI represent equity securities with a readily determinable fair value and are required to be measured at fair value at each reporting period using readily determinable pricing available on a securities exchange, in accordance with the provisions of ASU 2016-01, *Recognition and Measurement of Financial Assets and Liabilities*. Therefore, the Company categorized the investments as current assets. The investments in Vivasure do not have readily determinable fair values and are recorded at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for identical or similar investments of the same issuer. Additionally, as the investments in Vivasure are not readily marketable, the Company categorized the investments as non-current assets. As of December 31, 2021 and 2022, the carrying value of the investments in Vivasure was $398,000 and $2.5 million, respectively.

Fair Value of Financial Instruments

The Company applies ASC 820, *Fair Value Measurement ("ASC 820")*, which establishes a framework for measuring fair value and clarifies the definition of fair value within that framework. ASC 820 defines fair value as an exit price, which is the price that would be received for an asset or paid to transfer a liability in the Company's principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value hierarchy established in ASC 820 generally requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Observable inputs reflect the assumptions that market participants would use in pricing the asset or liability and are developed based on market data obtained from sources independent of the reporting entity. Unobservable inputs reflect the entity's own assumptions based on market data and the entity's judgments about the assumptions that market participants would use in pricing the asset or liability and are to be developed based on the best information available in the circumstances.

The carrying value of the Company's cash and cash equivalents, accounts receivable, prepaid expense, accounts payable and accrued expenses approximate fair value because of the short-term maturity of these financial instruments. In addition, the Company records its investment in Motus GI, marketable securities, and warrant liabilities at fair value. In addition, at December 31, 2022, the Company believed the carrying value of debt approximates fair value as the interest rates were reflective of the rate the Company could obtain on debt with similar terms and conditions. See Note 5 for additional information regarding fair value measurements.

The valuation hierarchy is composed of three levels. The classification within the valuation hierarchy is based on the lowest level of input that is significant to the fair value measurement. The levels within the valuation hierarchy are described below:

Level 1 — Assets and liabilities with unadjusted, quoted prices listed on active market exchanges. Inputs to the fair value measurement are observable inputs, such as quoted prices in active markets for identical assets or liabilities.

Level 2 — Inputs to the fair value measurement are determined using prices for recently traded assets and liabilities with similar underlying terms, as well as direct or indirect observable inputs, such as interest rates and yield curves that are observable at commonly quoted intervals.

Level 3 — Inputs to the fair value measurement are unobservable inputs, such as estimates, assumptions, and valuation techniques when little or no market data exists for the assets or liabilities.

Accounts Receivable and Allowance for Doubtful Accounts

Accounts receivable represent amounts due from customers. The allowance for doubtful accounts is recorded for estimated losses by evaluating various factors, including relative creditworthiness of each customer, historical collections experience and aging of the receivable. As of December 31, 2021 and 2022, an allowance for doubtful accounts was not deemed necessary.

Inventory

Inventory is stated at the lower of standard cost (which approximates actual cost on a first-in, first-out basis) and net realizable value. Net realizable value represents the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal and transportation. The Company analyzes its inventory levels and writes down inventory that has become obsolete or has a cost basis in excess of its expected net realizable value or inventory quantities in excess of expected requirements. Excess requirements are determined based on comparison of existing inventories to forecasted sales, with consideration given to inventory shelf life. Expired inventory is disposed of, and the related costs are recognized in cost of goods sold. As of December 31, 2021 and 2022, an impairment charge as a result of obsolete inventory was not deemed necessary.

Research and Development Prepayments, Accruals and Related Expenses

The Company incurs costs of research and development activities conducted by its third-party service providers, which include the conduct of preclinical and clinical studies. We are required to estimate our prepaid and accrued research and development costs at each reporting date. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with our service providers. The Company determines the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers, as to the progress or stage of completion of trials or services, as of the end of the reporting period, pursuant to contracts with the third parties and the agreed upon fee to be paid for such services. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are accepted by the Company or the services are performed. Accruals are recorded for the amounts of services provided that have not yet been invoiced.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized over the lesser of their useful life or the remaining life of the lease. When assets are retired or

otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Maintenance and repairs are charged to operations as incurred.

Asset category	Depreciable life
Manufacturing equipment	10 years
Office equipment	3 – 7 years
Research and development equipment	7 years

Leases

In February 2016, the FASB issued Accounting Standards Update No. 2016-02, *Leases (Topic 842) ("ASC 842")*, which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. On January 1, 2022, the Company adopted the new lease standard using the optional transition method under which comparative financial information will not be restated and the Company will continue to apply the provisions of the previous lease standard in its annual disclosures for the comparative periods. In addition, the new lease standard provides a number of optional practical expedients in transition. The Company elected the package of practical expedients. As such, the Company did not have to reassess whether expired or existing contracts are or contain a lease and did not have to reassess the lease classifications or reassess the initial direct costs associated with expired or existing leases.

The new lease standard also provides practical expedients for an entity's ongoing accounting. The Company elected the short-term lease recognition exemption under which the Company will not recognize right-of-use ("ROU") assets or lease liabilities for leases that are less than one year in duration. The Company elected the practical expedient to not separate lease and non-lease components for certain classes of assets (facilities).

Upon adoption on January 1, 2022, the Company recognized ROU assets of $2.6 million and lease liabilities of $2.9 million. The adoption of the new lease standard did not impact the Company's condensed consolidated statement of operations and comprehensive loss or its condensed consolidated statement of cash flows. The effect of the transition adjustment along with balances before, and after adoption is outlined below:

	Deferred lease liability	ROU Assets	Lease Liabilities
Balance – December 31, 2021	$ 241	$ —	$ —
ASC 842 Transition adjustment	(241)	2,612	2,853
Balance – January 1, 2022	$ —	$ 2,612	$ 2,853

The Company determines if an arrangement is a lease at inception. For the Company's operating leases, the ROU asset represents the Company's right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. ROU assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. Since all the lease agreements do not provide an implicit rate, the Company estimated an incremental borrowing rate in determining the present value of the lease payments. Operating lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or expectations regarding the terms. Variable lease costs such as operating costs and property taxes are expensed as incurred.

Debt Discount and Debt Issuance Costs

Debt discounts and debt issuance costs incurred in connection with the issuance of debt are capitalized and reflected as a reduction to the related debt liability. The costs are amortized to interest expense over the term of the debt using the effective-interest method.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future net undiscounted cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be

recognized is measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. The Company has not identified any such impairment losses to date.

Warrants

The Company evaluates its warrants to determine if the contracts qualify as liabilities in accordance with ASC 480-10, *Distinguishing Liabilities from Equity* and ASC 815, *Derivatives and Hedging*. If the warrant is determined to meet the criteria to be liability classified, the warrant liability is marked-to-market each balance sheet date and recorded as a liability, with the change in fair value recorded in the statements of operations and comprehensive loss as gain (loss) on fair value adjustment of warrant liability within other income or expense.

In bundled transactions, the proceeds received from any debt instruments and liability classified warrants are allocated to the warrant at fair value first, and the residual value is then allocated to the debt instrument. Upon conversion or exercise of a warrant that is subject to liability treatment, the instrument is marked to fair value at the conversion or exercise date and the fair value is reclassified to equity. Equity classified warrants are recorded within additional paid-in capital at the time of issuance at fair value as of the issuance date and are not subject to subsequent remeasurement.

Revenue Recognition

The Company recognizes revenue under the core principle according to ASC 606, *Revenue from Contracts with Customers (“ASC 606”),* to depict the transfer of control to the Company’s customers in an amount reflecting the consideration the Company expects to be entitled to. In order to achieve that core principle, the Company applies the following five step approach: (1) identify the contract with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when a performance obligation is satisfied.

The Company’s revenues are currently comprised of product revenue from the sale of FreeHold’s intracorporeal organ retractors, and partnership revenues from the Terumo Agreement related to the development and commercialization of Virtue SAB.

Product Revenues

Product revenues related to sales of FreeHold’s intracorporeal organ retractors are recognized at a point-in-time upon the shipment of the product to the customer, and there are no significant estimates or judgements related to estimating the transaction price. The product revenues consist of a single performance obligation, and the payment terms are typically 30 days. Product revenues are recognized solely in the United States.

Partnership Revenues

To date, the Company’s Partnership revenues related to the Terumo Agreement as further described in Note 3. In future periods, Partnership revenues may also include revenues related to the Medtronic Agreement as discussed in Note 4.

The Company assessed whether the Terumo Agreement fell within the scope of ASC 808, *Collaborative Arrangements (“ASC 808”)* based on whether the arrangement involved joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. The Company determined that the Terumo Agreement did not fall within the scope of ASC 808. The Company then analyzed the arrangement pursuant to the provisions of ASC 606 and determined that the arrangement represents a contract with a customer and is therefore within the scope of ASC 606.

The promised goods or services in the Terumo Agreement include (i) license rights to the Company’s intellectual property, and (ii) research and development services. The Company also has optional additional items in the Terumo Agreement which are considered marketing offers and are accounted for as separate contracts with the customer if such option is elected by the customer, unless the option provides a material right which would not be provided without entering into the contract. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources or (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct in the Terumo Agreement, the Company considered factors such as the stage of development

of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

The Company estimates the transaction price for the Terumo Agreement performance obligations based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration includes both fixed consideration and variable consideration. At the inception of the Terumo Agreement, as well as at each reporting period, the Company evaluates the amount of potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected amount method to estimate the amount expected to be received based on which method better predicts the amount expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

The Terumo Agreement contains development and regulatory milestone payments. At contract inception and at each reporting period, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect partnership revenues and earnings in the period of adjustment.

The Terumo Agreement also includes sales-based royalties and the license is deemed to be the predominant item to which the royalties relate. Accordingly, the Company will recognize royalty revenue when the related sales occur. To date, the Company has not recognized any royalty revenue under the arrangement.

The Company has determined that intellectual property licensed to Terumo and the research and development services to be provided through the premarket approval by the FDA for the in-stent restenosis (“ISR”) indication represent a combined performance obligation that is satisfied over time, and that the appropriate method of measuring progress for purposes of recognizing revenues relates to a proportional performance model that measures the proportional performance based on the costs incurred to date relative do the total costs expected to be incurred through the completion of the performance obligation. The Company evaluates the measure of progress at each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company receives payments from Terumo based on billing schedules established in the contract. Such billings for milestone related events have 10-day terms from the date the milestone is achieved, royalty payments are 20-day terms after the close of each quarter, any optional services are 20 days after receipt of an invoice and any sales of the SirolimusEFR are within 30 days after receipt of the shipping invoices. Upfront payments are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the right to consideration is unconditional.

Stock-Based Compensation

The Company applies ASC 718-10, *Compensation — Stock Compensation*, which requires the measurement and recognition of compensation expenses for all stock-based payment awards made to employees and directors including employee stock options under the Company’s stock plans based on estimated fair values (see Note 10). Each award vests over the subsequent period during which the recipient is required to provide service in exchange for the award (the vesting period). The cost of each award is recognized as an expense in the financial statements over the respective vesting period on a straight-line basis.

Under the requirements of ASU 2018-07, the Company accounts for stock-based compensation to nonemployees under the fair value method, which requires all such compensation to be calculated based on the fair value at the measurement date (generally the grant date) and recognized in the consolidated statements of operations and comprehensive loss over the requisite service period. The Company accounts for forfeitures of stock-based awards as they occur.

Net Loss Per Share

Basic and diluted net loss per share is calculated by dividing net loss per share by the weighted-average number of shares of common stock outstanding for the period, without consideration of potential dilutive shares of common stock. Since the Company was in a loss position for the periods presented, basic net loss attributable to common stockholders is the same as diluted net loss attributable to common stockholders since the effects of potentially dilutive securities are antidilutive. Potentially dilutive securities include all outstanding warrants, stock options, and restricted stock. In periods in which there is net income, the Company would apply the two-class method to compute net income per share. Under this method, earnings are allocated to common stock and participating securities based on their respective rights to receive dividends, as if all undistributed earnings for the period were distributed. The two-class method does not apply in periods in which a net loss is reported.

Income Taxes

The Company accounts for income taxes using the asset-and-liability method in accordance with ASC 740, *Income Taxes ("ASC 740")*. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on the deferred tax assets and liabilities of a change in tax rate is recognized in the period that includes the enactment date. A valuation allowance is recorded if it is more-likely-than-not that some portion or all the deferred tax assets will not be realized in future periods. At December 31, 2021 and 2022, the Company has recorded a full valuation allowance on its deferred tax assets.

The Company follows the guidance in ASC Topic 740-10 in assessing uncertain tax positions. The standard applies to all tax positions and clarifies the recognition of tax benefits in the financial statements by providing for a two-step approach of recognition and measurement. The first step involves assessing whether the tax position is more-likely-than-not to be sustained upon examination based upon its technical merits. The second step involves measurement of the amount to be recognized. Tax positions that meet the more-likely than-not threshold are measured at the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate finalization with the taxing authority. The Company recognizes the impact of an uncertain income tax position in the financial statements if it believes that the position is more likely than not to be sustained by the relevant taxing authority. The Company will recognize interest and penalties related to tax positions in income tax expense.

Deferred Offering and Merger Costs

Offering and merger costs, consisting of legal, accounting, printer and filing fees, are deferred and will be offset against proceeds received when the financing events are completed. In the event the offering or merger is terminated, all deferred costs will be expensed. As of December 31, 2022, the Company has capitalized $4.0 million of deferred merger costs related to the Business Combination discussed in Note 15, which are included in deposits and other assets on the accompanying balance sheet. As of December 31, 2021, the Company capitalized $100,000 of deferred offering costs related to private placement financings, which was offset against the proceeds received in March of 2022.

Defined Contribution Plan

The Company has a defined contribution retirement savings plan under Section 401(k) of the Internal Revenue Code. This plan allows eligible employees to defer a portion of their annual compensation on a pre-tax basis. The Company does not make matching employee contributions.

Comprehensive Loss

Comprehensive loss is comprised of net loss and changes in unrealized gains and losses on the Company's available-for-sale investments.

Segment Reporting

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company has determined it operates in one segment.

New Accounting Standards

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. During 2018 and 2019, the FASB also issued subsequent amendments to the initial guidance (collectively, "Topic 326"). Topic 326 requires organizations to measure all expected credit losses for financial instruments held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. Topic 326 will be effective for the Company on January 1, 2023. The Company is evaluating the impact that this standard will have on its consolidated financial statements.

In June 2022, the FASB issued ASU No. 2022-03 — *Fair Value Measurement (ASC 820): Fair Value Measurement of Equity Securities Subject to Contractual Sale Restrictions*, which clarifies that a contractual restriction on the sale of an equity security is not considered part of the unit of account of the equity security and, therefore, is not considered in measuring fair value. The Company adopted ASU 2022-03 in the second quarter of 2022, and the adoption did not have a material impact on the consolidated financial statements.

3. Terumo Agreement

In June 2019, the Company entered into the Terumo Agreement, pursuant to which Terumo secured global commercialization rights for Virtue SAB in coronary and peripheral vascular indications (the "Terumo Indications"). Under this agreement, the Company received an upfront payment of $30 million and an equity commitment of up to $5 million of which $2.5 million was invested in June 2019 as part of the Series B-1 financing. The Company was initially eligible to receive up to $65 million in additional payments based on the achievement of certain development and regulatory milestones and is also eligible to earn royalties on future sales by Terumo based on royalty rates ranging from 10 – 15%. As of the issuance date of these financial statements, the target achievement date for two $5 million milestone payments has already passed. In addition, due to delays in Orchestra's Virtue SAB program resulting from the COVID-19 pandemic, supply chain issues and unexpected changes to regulatory requirements, including increased testing and other activities related to chemistry, manufacturing, and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, Orchestra is unlikely to be able to complete the remaining time-based milestones by the specified target achievement dates to earn the remaining $25 million in time-based milestone payments pursuant to the Terumo Agreement. However, in June 2022, Orchestra and Terumo signed a letter agreement whereby the parties agreed to negotiate in good faith over 12 months mutually agreeable adjustments to certain target achievement dates to reflect the regulatory and pandemic-related delays. There is no assurance as to the outcome of these negotiations with respect to any potential modifications to the milestone target achievement dates. Pursuant to the terms of the Terumo Agreement, the Company licensed intellectual property rights to Terumo and the Company shall be primarily responsible for completing the development of the product in the United States through premarket approval by the FDA for the in-stent restenosis ("ISR") indication. These research and development services to be provided by the Company include (i) manufacturing, testing and packaging the drug required for the clinical trials, (ii) supplying Terumo with information related to the design and manufacture of the delivery device and the technology transfer needed for Terumo to ultimately commence manufacture of the delivery device, and (iii) carrying out regulatory activities related to clinical trials in the United States for the ISR indication.

The Company has concluded that the license granted to Terumo is not distinct from the research and development services that will be provided to Terumo through the completion of the development of ISR indication, as Terumo cannot obtain the benefit of the license without the related research and development services. Accordingly, the Company will recognize revenues for this combined performance obligation over the estimated period of research and development services using a proportional performance model. The Company measures proportional performance based on the costs incurred relative to the total estimated costs of the research and development services.

In 2019, the Company received a total of $32.5 million from Terumo related to the stock purchase and the revenue generating elements of the Terumo Agreement. The Company recorded the estimated fair value of the shares of $2.5 million in stockholders' equity, as the value paid by Terumo is consistent with the value paid by other third-party stockholders in the Company's offering of its Series B-1 Preferred Stock. The Company allocated the remaining $30 million to the transaction price of the Terumo Agreement. The Company considers the future potential development and regulatory milestones to be variable consideration, which are fully constrained from the transaction price as of December 31, 2021 and 2022, as the achievement of such milestone payments are uncertain and highly susceptible to factors outside of the Company's control. The Company plans to re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur. In addition, the arrangement also includes sales-based royalties on product sales by Terumo subsequent to commercialization ranging from 10 - 15%, none of which have been recognized to date.

The Company recorded the $30 million upfront payment received from Terumo in 2019 within deferred revenue. The following table presents the changes in the Company's deferred revenue balance from the Terumo Agreement during the years ended December 31, 2021 and 2022:

Deferred Revenue – January 1, 2021 (in thousands)	$	20,926
Revenue reduction		1,475
Deferred Revenue – December 31, 2021	$	22,401
Revenue recognized		(2,862)
Deferred Revenue – December 31, 2022	$	19,539

The Company's balance of deferred revenue contains the transaction price from the Terumo Agreement allocated to the combined license and research and development performance obligation, which was partially unsatisfied as of December 31, 2022. The Company expects to recognize approximately $6.4 million of its deferred revenue during the next twelve months and recognize the remaining approximately $13.1 million through the remainder of the performance period, which is estimated through 2026.

As of each quarterly reporting date, the Company evaluates its estimates of the total costs expected to be incurred through the completion of the combined performance obligation and updates its estimates as necessary. For the years ended December 31, 2021 and 2022, the expenses incurred related to the Terumo Agreement were approximately $9.9 million and $14.3 million, respectively. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 85% as of December 31, 2021 as compared to the estimates as of December 31, 2020, and increased by approximately 10% as of December 31, 2022, as compared to the estimates as of December 31, 2021. The increase in the estimated costs relates to an extension of the estimated performance period by twelve months, due in part by delays resulting from the COVID-19 pandemic, as well as supply chain issues and unexpected changes to regulatory requirements, including increased testing and other activities related to chemistry, manufacturing, and control, increased nonclinical and good laboratory practice preclinical data requirements, including biocompatibility, as well as a requirement to repeat good laboratory practice preclinical studies already performed based on changes to source of component materials and a change in manufacturing site, that caused the Company to amend its original project plan. While the Company believes it has estimated total costs associated with the Terumo Agreement through completion, these estimates encompass a broad range of expenses over a multi-year period and, as such, are subject to periodic changes as new information becomes available. The impact of the changes in estimates resulted in reduction of partnership revenues of $6.5 million and $1.0 million for the years ended December 31, 2021 and 2022, respectively, as compared to the amounts that would have been recorded based on the previous estimates. The impact of these changes in estimates on the net loss per share attributable to common stockholders, basic and diluted, was an increase of $0.73 and $0.07 for the years ended December 31, 2021 and 2022, respectively.

Orchestra will also manufacture, or have manufactured, SirolimusEFR and have exclusive rights to sell it on a per unit basis to Terumo for use in the Virtue SAB product. The Company has determined that this promise does not contain a material right as the pricing is based on standalone selling prices. Through December 31, 2022, there have been no additional amounts recognized as revenue under the Terumo Agreement other than the recognition of a portion of the upfront payment described above.

4. Medtronic Agreement

In June 2022, Orchestra, BackBeat Medical, LLC and Medtronic, Inc. (an affiliate of Medtronic plc) ("Medtronic") entered into the Medtronic Agreement for the development and commercialization of BackBeat CNT for the treatment of hypertension ("HTN") in patients indicated for a cardiac pacemaker (the "Primary Field"). Under the terms of the Medtronic Agreement, Orchestra will sponsor

a multinational pivotal study to support regulatory approval of BackBeat CNT in the Primary Field and be financially responsible for development, clinical and regulatory costs associated with this pivotal study. Medtronic is currently working with Orchestra to integrate BackBeat CNT into its top-of-the-line, commercially available dual-chamber pacemaker system for use in the pivotal trial and will provide development, clinical and regulatory resources in support of the pivotal trial, for which Orchestra will reimburse Medtronic at cost.

Under the terms of the Medtronic Agreement, Medtronic will have exclusive rights to commercialize BackBeat CNT-enabled pacing systems globally following receipt of regulatory approval. Medtronic would be entirely responsible for global commercialization following receipt of regulatory approvals, including manufacturing, sales, marketing and distribution costs.

Orchestra is expected to receive between $500 and $1,600 per BackBeat CNT enabled device sold based on a formula of the higher of (1) a fixed dollar amount per BackBeat CNT-enabled device (amount varies materially on a country-by-country basis) or (2) a percentage of the BackBeat CNT generated sales. Procedures using the BackBeat CNT-enabled pacemakers are expected to be billed under existing reimbursement codes.

Medtronic has a right of first negotiation through FDA approval of BackBeat CNT in the Primary Field, to expand its global rights to BackBeat CNT for the treatment of HTN patients not indicated for a pacemaker.

The Company assessed whether the Medtronic Agreement fell within the scope of ASC 808 and concluded that the Medtronic Agreement fell within the scope of ASC 808. In addition, the Company determined that Medtronic is a customer for a good or service that is a distinct unit of account, and therefore, the transactions in the Medtronic Agreement should be accounted for under ASC 606.

The Company has concluded that the license granted to Medtronic is not distinct from the development and implementation services that will be provided to Medtronic through the completion of the development of HTN indication, as Medtronic cannot obtain the benefit of the license without the related development and implementation services. ASC 606-10-55-65 includes an exception for the recognition of revenue relating to licenses of intellectual property with sales-based or usage-based royalties. Under this exception, royalty revenue is not recorded until the subsequent sale or usage occurs, or the performance obligation has been satisfied, whichever is later.

The Company concluded that the exemption applies and therefore, the royalty revenue associated with these performance obligations will be recognized as the underlying sales occur. Additionally, pursuant to the Medtronic Agreement, expenses incurred by Medtronic in connection with clinical device development and regulatory activities performed will be reimbursed by Orchestra. The Company will record such expenses as research and development expenses as incurred. During the year ended December 31, 2022, the Company incurred approximately $1.7 million of research and development costs related to these reimbursements to the Medtronic Agreement, all of which is included within accounts payable and accrued expenses in the December 31, 2022 consolidated balance sheet.

Concurrently with the close of the Medtronic Agreement, Orchestra also received a $40 million investment from Medtronic in connection with a private placement financing. The equity was purchased at a fair value consistent with the price paid by other investors at that time, and accordingly, the proceeds received were recorded as an equity investment.

Through December 31, 2022, there have been no amounts recognized as revenue under the Medtronic Agreement.

5. Financial Instruments and Fair Value Measurements

The following tables summarize the Company's financial assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy:

(in thousands)	December 31, 2021 Level 1	Level 2	Level 3	Total
Assets				
Investment in Motus GI (see Note 6)	$ 958	$ —	$ —	$ 958
Total assets	$ 958	$ —	$ —	$ 958
Liabilities:				
Warrant liability (see Note 9)	$ —	$ —	$ 635	$ 635
Total liabilities	$ —	$ —	$ 635	$ 635

(in thousands)	December 31, 2022 Level 1	Level 2	Level 3	Total
Assets				
Investment in Motus GI (see Note 6)	$ 86	$ —	$ —	$ 86
Marketable securities (Corporate and Government debt securities)	—	63,915	—	63,915
Total assets	$ 86	$ 63,915	$ —	$ 64,001
Liabilities:				
Warrant liability (see Note 9)	$ —	$ —	$ 2,089	$ 2,089
Total liabilities	$ —	$ —	$ 2,089	$ 2,089

The Company's warrant liability is measured at fair value on a recurring basis using unobservable inputs and are classified as Level 3 inputs, and any change in fair value is recognized as change in fair value of warrant liability in the consolidated statements of operations and comprehensive loss. Refer to Note 8 for the valuation technique and assumptions used in estimating the fair value of the warrants.

The Level 2 assets consist of government and corporate debt securities which are valued using market observable inputs, including the current interest rate and other characteristics for similar types of investments, whose fair value may not represent actual transactions of identical securities. There were no transfers between Levels 1, 2 or 3 for the periods presented.

6. Marketable Securities and Strategic Investments

Marketable Securities

The following is a summary of the Company's marketable securities as December 31, 2022:

(in thousands)	December 31, 2022 Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 52,242	$ 7	$ —	$ 52,249
Government debt securities	11,681	—	(15)	11,666
Total	$ 63,923	$ 7	$ (15)	$ 63,915

As of December 31, 2021, there were no marketable securities held. For the years ended December 31, 2021 and 2022, the Company did not recognize any realized gains or losses on its marketable securities.

Strategic Investments

The Company values the Motus GI investment by measuring fair value using the listed share price on the Nasdaq Capital Market on each valuation date.

Aggregate losses of $1.0 million and $0.9 million during the years ended December 31, 2021 and 2022, respectively, were recorded to adjust the strategic investments in equity securities of Motus GI to its fair value of $1.0 million at December 31, 2021 and $86,000 at December 31, 2022, which is classified as strategic investments within current assets on the accompanying consolidated balance sheet.

The Company's long term strategic investments as of December 31, 2022 represent investments made in Vivasure in 2020, 2021 and 2022 that were originally recorded at cost. There were no observable price changes or impairments identified during the year ended December 31, 2021 related to these investments.

In May 2022, Vivasure announced a Series D private placement, in which it received a material investment from a new strategic investor. As a result, the Company's existing convertible redeemable notes converted into Series D Preferred Stock of Vivasure in May 2022. The investment in the Vivasure Series D Preferred Stock represents an observable price change in an orderly transaction for an identical instrument of the same issuer, and accordingly, the Company recognized a gain on its strategic investment in Vivasure of $1.9 million in the second quarter of 2022. This amount represents a portion of the previously impaired investment balance described below.

During the fourth quarter of 2019, the Company identified indicators of impairment of Vivasure strategic investments held at that time as a result of adverse changes in Vivasure's business operations, including liquidity concerns. As a result, the Company recorded an impairment charge in the fourth quarter of 2019 of $5.8 million, which represents the cumulative impairment charges recorded on Vivasure strategic investments to date.

7. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following:

(in thousands)	December 31, 2021	December 31, 2022
Equipment	$ 1,207	$ 1,712
Office furniture	305	364
Leasehold improvements	177	191
Construction in progress	16	—
Property and equipment, gross	1,705	2,267
Less accumulated depreciation and amortization	(585)	(778)
Total Property and equipment, net	$ 1,120	$ 1,489

Depreciation and amortization expense was $181,000 and $222,000 for the years ended December 31, 2021 and 2022, respectively.

Accrued Expenses

Accrued expenses consist of the following:

(in thousands)	December 31, 2021	December 31, 2022
Accrued compensation	$ 1,319	$ 2,480
Deferred offering and merger costs	100	—
Deferred lease liability	45	—
Clinical trial accruals	39	1,003
Other accrued expenses	531	1,893
Total accrued expenses	$ 2,034	$ 5,376

8. Warrants

The Company evaluates its outstanding warrants to determine if the instruments qualify for equity or liability classification. To date, the majority of the Company's warrants are required to be accounted for as liabilities, and therefore, the fair value of the warrant liability is marked-to-market at each balance sheet date, with the change in fair value recorded in the statements of operations and comprehensive loss within other income (expense). Upon conversion or exercise of a warrant classified as a liability, the instrument is marked to fair value at the conversion date and then that fair value is reclassified to equity.

The Company calculates the fair value of the outstanding warrant liability at each reporting date by estimating the equity value of the Company, and then utilizing option pricing models to allocate the total equity value to the shares and warrants outstanding. The inputs used in the valuation models for Orchestra's warrant liability are as follows:

	December 31,	
	2021	2022
Expected volatility	44 – 55%	45 – 47%
Risk-free interest rate	0.27 – 1.11%	4.00 – 4.30%
Remaining term in years	1.41 – 7.94	0.14 – 5.07
Exercise price of common warrants	$1.08 – $30.11	$1.08 – $30.11
Exercise price of preferred warrants	$19.35 – $32.26	—
Common stock price	$3.35	$9.72
Preferred stock price	$5.38 – $7.35	—
Expected dividend yield	0%	0%

The Company's warrant liability activity rollforward is as follows:

(in thousands, except share data)	Preferred Warrants	Common Warrants	Amount
Balance December 31, 2020	206,997	1,192,650	$ 1,347
Exercise of warrants	—	(3,488)	(13)
Change in the fair value of warrants	—	—	(699)
Balance December 31, 2021	206,997	1,189,162	$ 635
Reclassification of warrant liability upon exercise	—	(73,238)	(171)
Forfeiture of warrants	—	(4,650)	(38)
Issuance of warrants related to private placement financing	—	159,965	620
Amendment of existing warrants	(206,997)	206,997	810
Other	—	(151,162)	(345)
Change in the fair value of warrants	—	—	578
Balance December 31, 2022	—	1,327,074	$ 2,089

In June 2022, concurrent with the close of a private placement financing, the Company amended the terms of certain existing warrant agreements, which included modifying the underlying shares of the warrants from preferred warrants to common warrants and reducing the strike prices. Such amendments resulted in $0.8 million of additional expense for the year ended December 31, 2022.

As of December 31, 2022, the Company has 250,000 warrants classified within equity with strike prices ranging from $1.33 — $4.06 and remaining terms in years of 6.94 — 9.50. The equity classified warrants were recorded within additional paid-in capital at the time of issuance at fair value and are not subject to subsequent remeasurement.

9. Stock-Based Compensation

Stock-based Compensation — Orchestra BioMed 2018 Stock Incentive Plan

As of December 31, 2022, all stock-based awards were outstanding under a single equity incentive plan, the Orchestra BioMed, Inc. 2018 Stock Incentive Plan (the "Plan"). Under the Plan, up to 5.2 million shares of the Company's common stock may be issued pursuant to awards granted in the form of nonqualified stock options, restricted and unrestricted stock awards, and other stock-based

awards. Employees, consultants, and directors are eligible for awards granted under the plan which generally have a contractual life of up to 10 years and may be exercisable in cash or as otherwise determined by the board of directors. Vesting generally occurs over a period of not greater than three years.

Total stock-based compensation related to option issuances was as follows:

(in thousands)	Year ended December 31, 2021	Year ended December 31, 2022
Research and development	$ 83	$ 398
Selling, general and administrative	88	2,704
Total stock-based compensation	$ 171	$ 3,102

As of December 31, 2022, there was approximately $7.2 million of unrecognized stock-based compensation expense associated with the stock options noted above that is expected to be recognized over a weighted average period of three years.

Total restricted stock-based compensation was as follows:

(in thousands)	Year ended December 31, 2021	Year ended December 31, 2022
Research and development	$ —	$ —
Selling, general and administrative	131	273
Total stock-based compensation	$ 131	$ 273

As of December 31, 2022, there was approximately $408,000 of unrecognized restricted stock-based compensation expense associated with the restricted stock noted above that is expected to be recognized over a weighted average period of approximately 3 years.

The following table summarizes the stock option activity of the Company under the Plan:

	Shares Underlying Options	Weighted Average Exercise Price	Weighted Average Remaining Term (years)	Aggregate Intrinsic Value (thousands)
Outstanding at January 1, 2022	1,348,464	4.47	7.13	—
Granted	2,357,807	9.33	—	—
Exercised	(27,848)	4.32	—	—
Forfeited/canceled	(19,595)	4.67	—	—
Outstanding December 31, 2022	3,658,828	7.56	8.35	$ 8,277
Exercisable at December 31, 2022	1,806,093	5.78	6.72	$ 6,815

The following table summarizes the restricted stock activity of the Company under the Plan:

	Restricted Stock Outstanding	Weighted Average Remaining Term (years)	Aggregate Intrinsic Value (thousands)
Outstanding January 1, 2022	21,907	7.60	—
Granted	182,962	9.15	—
Vested	(46,280)	—	—
Forfeited/canceled	—	—	—
Outstanding December 31, 2022	158,589	9.14	$ 980

During the year ended December 31, 2022, the Company granted 182,961 restricted stock awards ("RSAs") at a weighted-average grant date fair value of $3.61 while 46,281 RSAs vested at a weighted-average grant date fair value of $3.12.

Determination of Fair Value

The estimated grant-date fair value of all the Company's option awards was calculated using the Black-Scholes option pricing model, based on the following weighted average assumptions:

	Year ended December 31,	
	2021	2022
Expected term (in years)	6.00	6.00
Expected volatility	60 %	50 %
Risk-free interest rate	0.99 %	3.01 %
Expected dividend yield	0 %	0 %
Fair value of common stock	$ 4.71	$ 9.72

The fair value of each stock option grant was determined by the Company using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

Expected Term — The expected term represents the period that stock-based awards are expected to be outstanding. The Company's historical share option exercise information is limited due to a lack of sufficient data points and did not provide a reasonable basis upon which to estimate an expected term. The expected term for option grants is therefore determined using the "simplified" method, as prescribed in the Securities and Exchange Commission's Staff Accounting Bulletin (SAB) No. 107. The simplified method deems the expected term to be the midpoint between the vesting date and the contractual life of the stock-based awards.

Expected Volatility — The expected volatility was derived from the historical stock volatilities of comparable peer public companies within the Company's industry that are considered to be comparable to the Company's business over a period equivalent to the expected term of the stock-based awards since there has been no trading history of the common stock.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the stock-based awards' expected term.

Expected Dividend Yield — The expected dividend yield is zero as the Company has not paid nor does it anticipate paying any dividends on its common stock in the foreseeable future.

Fair Value of Common Stock — As the Company's common stock has not historically been publicly traded, its board of directors periodically estimated the fair value of the Company's common stock considering, among other things, contemporaneous valuations of its common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

10. Leases

Office Lease

In August 2019, the Company entered into an addendum to the original December 2009 lease agreement for 8,052 square feet of office space in New Hope, PA. The lease will expire in September 2024. Monthly fees will be between $9,000 and $19,000 for the period from commencement through termination.

In November 2019, the Company entered into a new lease agreement for approximately 5,200 square feet of office space in New York, NY. The lease will expire in March 2028. Monthly fees will be between $28,000 and $30,000 for the period from commencement through termination.

In January 2020, the Company entered into an agreement for the use of portions of the office space of Motus GI, a related party, in Fort Lauderdale, Florida. The agreement will expire in September 2024. The monthly fee commenced on the month following the date of agreement. Monthly fees will be between $12,000 and $17,000 for the period from commencement through termination.

In May 2022, the Company amended the agreement with Motus GI for a larger portion of the office space and extended the expiration date to November 2024. Monthly fees will be between $7,000 and $23,000 for the period from commencement of the amendment to expiration. The amount paid is estimated to be proportionate to the percentage of space used by the Company applied to the monthly rent obligated to be paid by Motus GI to their landlord.

Operating cash flow supplemental information for the year ended December 31, 2022:

An initial right-of-use asset of $2.6 million was recognized as an asset and operating lease liabilities of $2.9 million was recognized as a liability upon the adoption of the new lease standard. Cash paid for amounts included in the present value of operating lease liabilities was $702,000 during the year ended December 31, 2022.

As of December 31, 2022:	
Weighted average remaining lease term – operating leases, in years	4.06
Weighted average discount rate – operating leases	6.25 %

Operating Leases

Rent/lease expense for office and lab space was approximately $697,000 and $735,000 for the years ended December 31, 2021 and 2022 respectively. The table below shows the future minimum rental payments, exclusive of taxes, insurance and other costs, under the leases as of December 31, 2022:

Year ending December 31:	Operating Leases (in thousands)
2023	$ 823
2024	727
2025	352
2026	352
2027	352
Thereafter	88
Total future minimum lease payments	$ 2,694
Imputed interest	(314)
Total liability	$ 2,380

11. Income Taxes

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company’s deferred tax assets relate primarily to its net operating loss carryforwards and other balance sheet basis differences. In accordance with ASC 740, *Income Taxes*, the Company recorded a valuation allowance to fully offset the gross deferred tax asset, because it is not more likely than not that the Company will realize future benefits associated with these deferred tax assets at December 31, 2021 and 2022.

The change in the valuation allowance for the years ended December 31, 2021 and 2022 was an increase of $7.2 million and $8.8 million, respectively.

In general, the U.S. Federal and state income tax returns remain open to examination by taxing authorities for tax years beginning in 2018 to present. However, if the Company claims net operating loss (“NOL”) carryforwards from years prior to 2018 against future taxable income, the tax returns pertaining to those losses may be examined by the taxing authorities.

The components of the deferred tax assets are as follows:

(in thousands)	December 31, 2021	December 31, 2022
Deferred tax assets		
Net operating loss carryovers – Federal	$ 19,936	$ 22,798
Net operating loss carryovers – State	5,640	4,811
Unrealized loss on equity securities	2,415	2,913
Research and development credits	2,300	3,149
Loss on impairment of strategic investments	1,449	1,177
Research and experimental costs	—	4,973
Other	552	1,478
Lease liability	—	629
Deferred revenue	5,353	5,166
Total deferred tax assets	37,645	47,094
Less: valuation allowance	(37,630)	(46,457)
Total deferred tax assets	15	637
Deferred tax liabilities		
Right-of-use asset	—	(578)
Depreciation and amortization	(15)	(59)
Total deferred tax liabilities	(15)	(637)
Total net deferred tax asset	$ —	$ —

Reconciliation of the statutory federal income tax to the Company's effective tax is as follows:

	December 31, 2021	December 31, 2022
Income tax benefit at federal statutory rate	21.0 %	21.0 %
State and local income tax (net of Federal benefit)	7.2 %	4.8 %
Permanent items	0.6 %	(0.9)%
Research and development credits	1.9 %	3.1 %
Research and development, uncertain tax positions	(0.4)%	(0.6)%
Change in valuation allowance	(31.2)%	(26.2)%
Effect of rate changes	— %	(1.2)%
True-ups	0.9 %	— %
Other	— %	— %
Effective tax rate	— %	— %

The Company had approximately $108.6 million and $88.0 million of gross NOL carryforwards (Federal and state, respectively) and approximately $3.1 million of Federal research and development tax credits, respectively, as of December 31, 2022, after applying Section 382 and Section 383 limitations. The federal net operating losses for years ending on or before December 31, 2017 start to expire from 2027 to 2037. The federal net operating losses generated after the year ended December 31, 2017 have an indefinite carryforward period, subject to 80% taxable income limitation on an annual basis. Certain state net operating losses start to expire in 2027, and certain states have an indefinite carryforward period. The federal research and development ("R&D") tax credit starts to expire from 2028 to 2042.

The NOL carryforwards and R&D tax credits are available to reduce future taxable income. However, Sections 382 and 383 of the Internal Revenue Code, and similar state regulations, contain provisions that may limit the NOL carryforwards and R&D tax credits available to be used to offset income in any given year upon the occurrence of certain events, including changes in the ownership interests of significant stockholders. In the event of a cumulative change in the ownership interest of significant stockholders in excess of 50% over a three-year period, the amount of the NOL carryforwards and R&D tax credits that the Company may utilize in any one year may be limited. In 2019, the Company completed Section 382 and Section 383 studies. As a result of these studies, the federal net operating loss and federal R&D tax credit carryforwards were reduced to reflect the amounts that are estimated to not be limited under the provisions of Sections 382 and 383. In 2019, the Company performed an analysis of the impact of ownership changes on state net operating loss carryforwards and provisional amounts were recorded within the income tax provision.

The Tax Cuts and Jobs Act resulted in significant changes to the treatment of research and experimental expenditures under Section 174. For tax years beginning after December 31, 2021, taxpayers are required to capitalize and amortize these expenditures that are paid or incurred in connection with their trade or business. Specifically, costs for U.S.-based research and experimental activities must be amortized over five years and costs for foreign research and experimental activities must be amortized over 15 years—both using a midyear convention. During the year ended December 31, 2022, the Company recorded a deferred tax asset of $5.0 million for such costs.

In assessing the realizability of the net deferred tax asset, the Company considers all relevant positive and negative evidence in determining whether it is more likely than not that some portion or all of the deferred income tax assets will not be realized. The realization of the gross deferred tax assets is dependent on several factors, including the generation of sufficient taxable income prior to the expiration of the net operating loss carryforwards. Management believes it is more likely than not that the Company's deferred income tax assets will not be realized. As such, the Company has provided a 100% valuation allowance on its net deferred tax assets as of December 31, 2021 and 2022.

Following is a reconciliation of beginning and ending balances of total amounts of gross unrecognized tax benefits:

(in thousands)	December 31, 2021	December 31, 2022
Unrecognized tax benefits		
Unrecognized tax benefits at the beginning of the period	$ 481	$ 572
Additions due to current year activity	111	203
Other reductions	(20)	—
Unrecognized tax benefits at the end of the period	$ 572	$ 775

The total liabilities associated with the unrecognized tax benefits that, if recognized, would impact the Company's effective tax rate were $572,000 and $775,000 at December 31, 2021 and 2022, respectively. It is not anticipated that the balance of unrecognized tax benefits at December 31, 2022 will change significantly over the next twelve months. The balance of unrecognized tax benefits as reflected in the table above are recorded on the balance sheet as a reduction to the related deferred tax asset in accordance with ASU 2013-11.

The Company's policy is to recognize interest accrued and, if applicable penalties related to unrecognized tax benefits in income tax expense for all periods presented. No interest or penalties were recognized during 2021 or 2022.

On December 27, 2020, the Consolidated Appropriations Act 2021 (the "Appropriations Act") was enacted in response to the COVID-19 pandemic. The Appropriations Act, among other things, temporarily extends through December 31, 2025, certain expiring tax provisions. Additionally, the Appropriations Act enacts new provisions and extends certain provisions originated within the Coronavirus Aid, Relief, and Economic Security Act, enacted on March 27, 2020. The accounting is now complete. On March 11, 2021, the American Rescue Plan ("ARP") was signed into law. Management has evaluated the impact of the law and does not expect the ARP would result in any tax or cash benefits.

On August 16, 2022, the Inflation Reduction Act of 2022 (“IRA”) was signed into law. The IRA made several changes to the U.S. tax code effective after December 31, 2022, including, but not limited to, a 15% minimum tax on large corporations with average annual financial statement income of more than $1 billion for a three tax-year period and a 1% excise tax on public company stock buybacks, which will be accounted for in treasury stock. We do not expect these changes to have a material impact on our provision for income taxes or financial statements.

12. Related Party Transactions

In addition to transactions and balances related to cash and stock-based compensation to officers and directors, the Company had the following transactions and balances with related parties and executive officers during 2021 and 2022:

Vivasure Investments

In December 2020 and 2021, and April 2022, the Company invested in Vivasure, a related party, $183,000, $213,000 and $208,000, respectively, in the form of unsecured convertible redeemable notes. The unsecured convertible redeemable notes converted into Series D preferred stock of Vivasure in May of 2022 (Note 6).

13. Debt Financing

In December 2019, the Company entered into a Loan and Security Agreement with Silicon Valley Bank (the “2019 Loan and Security Agreement”). The terms of the 2019 Loan and Security Agreement include a term loan of $20 million available in two tranches. The first $10 million tranche is available to the Company with interest-only monthly payments during a 12-month draw period from December 2019 through December 31, 2020. On December 31, 2020, the Company borrowed the first $10 million tranche of the 2019 Loan and Security Agreement.

Pursuant to the terms of the 2019 Loan and Security Agreement, the Company issued Silicon Valley Bank a warrant that, to the extent the Company draws on the 2019 Loan and Security Agreement, will be exercisable for a number of shares of common stock equal to 2% of the amount drawn under the 2019 Loan and Security Agreement divided by the exercise price of $1.33 per share. As a result of the draw in December of 2020, the Company issued 150,000 common stock warrants to Silicon Valley Bank, and the estimated fair value of the warrants of $544,000 was recorded as debt discount on the date of issuance and is being amortized to interest expense over the term of the credit facility.

The term loan accrues interest at a floating per annum rate equal to the greater of (i) the Wall Street Journal prime rate plus 1.00% or (ii) 6.25%. In addition, there is a final payment equal to 8.25% of the original aggregate principal amount which will be accrued over the term of the loan using the effective-interest method.

The term loan is secured by all of the Company’s assets, excluding intellectual property and certain other assets. The loan contains customary affirmative and restrictive covenants, including the Company’s ability to enter into fundamental transactions, incur additional indebtedness, grant liens, pay any dividend or make any distributions to its holders, make investments, merge or consolidate with any other person or engage in transactions with the Company’s affiliates, but does not include any financial covenants.

In June 2022, the Company entered into a Loan and Security Agreement with Avenue Venture Opportunities Fund I and II (the “2022 Loan and Security Agreement”). The terms of the 2022 Loan and Security Agreement include a term loan of up to $20 million available in two tranches with the first tranche of $10 million that was drawn at closing in June of 2022, and a second tranche of $10 million available at closing of the Series D-2 that has not yet been drawn. Additionally, the Company may have access to a third tranche of $30 million subject to certain financing milestones. The term loan matures on June 1, 2026. In addition, the lender has the right, at their discretion, but not the obligation, to convert any portion of the outstanding principal amount of the loans up to $5 million into shares of the Company’s common stock at a price per share equal to $12.00 (the “Conversion Option”), subject to adjustment; provided, however, the Conversion Option shall not be exercised by lender during the six (6) month period after completion of a Qualified SPAC (as defined in the 2022 Loan and Security Agreement). Concurrent with the closing of the 2022 Loan and Security Agreement, the Company terminated and repaid their existing 2019 Loan and Security Agreement, which resulted in a loss on extinguishment of $682,000.

Pursuant to the terms of the 2022 Loan and Security Agreement, the Company issued Avenue Venture Opportunities Fund I and II warrants that will be exercisable for 100,000 shares of common stock, and the estimated fair value of the warrants of $178,000 was recorded as debt discount on the date of issuance and is being amortized to interest expense over the term of the Loan and Security Agreement. In addition, other financing costs totaling $405,000 were also recorded as debt discount and is being amortized to interest expense over the term of the facility.

The term loan accrues interest at a floating per annum rate equal to the Wall Street Journal prime rate plus 6.45%. The rate in effect at December 31, 2022 was 13.45%. Total interest expenses recorded on the facility during the year ended December 31, 2022 was approximately $711,000. The repayment terms of the loan include monthly payments over a 4-year period, consisting of an initial 2 year interest-only period, followed by 24 monthly principal payments of $417,000 plus interest. In addition, there is a final payment equal to 4.25% of the initial commitment amount of $20 million, which will be accrued over the term of the loan using the effective-interest method.

	Principal Payments (in thousands)
Period ending December 31:	
2023	$ —
2024	2,500
2025	5,000
2026	2,500
Total	$ 10,000

The term loan is secured by all of the Company’s assets, excluding intellectual property and certain other assets. The loan contains customary affirmative and restrictive covenants, including the Company’s ability to enter into fundamental transactions, incur additional indebtedness, grant liens, pay any dividend or make any distributions to its holders, make investments, merge or consolidate with any other person or engage in transactions with the Company’s affiliates, but does not include any financial covenants.

14. Subsequent Events

On January 26, 2023 (the “Closing Date”), the Company consummated the previously-announced Business Combination (the “Closing”). In connection with the Business Combination, HSAC2 changed its jurisdiction of incorporation from the Cayman Islands to the State of Delaware and changed its name to “Orchestra BioMed Holdings, Inc.” (“New Orchestra”). On the Closing Date, Merger Sub merged with and into Orchestra with Orchestra being the surviving corporation and a wholly owned subsidiary of New Orchestra. The Company refers to HSAC2 common stock, after giving effect to the Business Combination, as “New Orchestra Common Stock.”

Upon the Closing, based on a ratio (the “Exchange Ratio”) of 0.465 shares of HSAC2 Common Stock for each whole share of Orchestra common stock, par value $0.0001 per share (the “Orchestra Common Stock”), 20,191,338 shares of New Orchestra Common Stock were issued to Orchestra stockholders (exclusive of the additional shares subject to earnout discussed below in this paragraph) and 5,523,834 shares of New Orchestra Common Stock were reserved for issuance pursuant to the Orchestra stock options and warrants converted into New Orchestra stock options and warrants in the Merger. In addition, upon the Closing, all of the Company’s outstanding preferred stock automatically converted New Orchestra Common Stock.

In connection with the Business Combination, HSAC 2 Holdings, LLC (the “Sponsor”) agreed that 25% or 1,000,000 shares of its New Orchestra Common Stock will be forfeited to New Orchestra on the first business day following the fifth anniversary of the Closing unless, as to 500,000 shares, the volume-weighted average price of the New Orchestra Common Stock is greater than or equal to $15.00 per share over any 20 trading days within any 30-trading day period (the “Initial Milestone Event”), and as to the remaining 500,000 shares, the volume-weighted average price of the New Orchestra Common Stock is greater than or equal to $20.00 per share over any 20 trading days within any 30-trading day period (the “Final Milestone Event”). Further, the Sponsor and HSAC2’s other initial shareholders prior to HSAC2’s initial public offering (the “IPO”) agreed to subject (i) the 4,000,000 shares of New Orchestra Common Stock issued to HSAC2’s initial shareholders prior to the IPO (the “Insider Shares”) and (ii) the 450,000 shares of New Orchestra Common Stock purchased in a private placement simultaneously with the IPO (the “Private Shares”) to a lock-up for up to 12 months following the Closing, and the Sponsor forfeited 50% of its 1,500,000 warrants in HSAC2 purchased upon consummation of the IPO (the “Private Warrants”), comprising 750,000 Private Warrants, for no consideration, immediately prior to the Closing (the “Sponsor Forfeiture”). Pursuant to the terms of the Merger Agreement, immediately following the Sponsor Forfeiture and prior to the Closing, HSAC2 issued 750,000 warrants to purchase New Orchestra Common Stock to eleven specified employees and directors of Orchestra. These new warrants have substantially similar terms to the forfeited Private Warrants, except that they will become exercisable between 24 and 36 months after the Closing.

In connection with the Business Combination, existing Orchestra stockholders also had the opportunity to elect to participate in an earnout (the “Earnout”) pursuant to which each such electing stockholder (an “Earnout Participant”) may receive a portion of additional contingent consideration of up to 8,000,000 shares of New Orchestra Common Stock in the aggregate (“Earnout Consideration”). Approximately 91% of Orchestra stockholders elected to participate in the Earnout. Each Earnout Participant agreed to extend their applicable lock-up period from 6 months to 12 months, pursuant to an Earnout Election Agreement and such Earnout Participants will collectively be entitled to receive: (i) 4,000,000 shares of the Earnout Consideration, in the aggregate, in the event that, from the time beginning immediately after the Closing until the fifth anniversary of the Closing Date (the “Earnout Period”), the Initial Milestone Event (as defined below) occurs; and (ii) an additional 4,000,000 shares of the Earnout Consideration, in the aggregate, in the event that, during the Earnout Period, the Final Milestone Event occurs.

Prior to the Business Combination, HSAC2’s public shares were listed on The Nasdaq Capital Market under the symbol “HSAQ.” On January 27, 2023, the New Orchestra Common Stock began trading on The Nasdaq Global Market under the symbol “OBIO.”

On August 8, 2023, the Company announced that the FDA granted investigational device exemption approval with conditions to initiate the Company’s planned Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with Coronary ISR. The Company is permitted to begin enrollment of the study upon completion of standard clinical trial initiation activities including clinical center Institutional Review Board approvals. The conditional approval also requires the Company to submit additional information to the FDA.

On September 19, 2023, the Company announced that the FDA granted investigational device exemption approval to initiate the Company’s planned BACKBEAT pivotal study evaluating the efficacy and safety for the development and commercialization of BackBeat CNT, also known as Atrioventricular Interval Modulation (AVIM) therapy for hypertensive pacemaker patients. The Company is permitted to begin enrollment upon completion of standard clinical trial initiation activities, including clinical center Institutional Review Board approvals. The Company expects to begin enrollment in the BACKBEAT pivotal study before the end of 2023.

On October 6, 2023, the Company repaid and terminated the 2022 Loan and Security Agreement. In connection with the repayment and termination, the Company repaid $10 million of principal and issued warrants to purchase 27,707 shares of Company Common Stock at an exercise price of $7.67 per share in lieu of a cash payment of approximately $212,500 due with respect to certain fees under the 2022 Loan and Security Agreement. The Company also paid approximately $849,000 of net interest, prepayment fees, and legal fees.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the estimated expenses to be borne by Orchestra BioMed Holdings, Inc. (the “Registrant”) in connection with the issuance and distribution of the shares of Common Stock being registered hereby. The security holders will not bear any portion of such expenses. All amounts shown are estimates except for the registration fee.

Securities and Exchange Commission registration fee	$	25,463
Legal fees and expenses	$	300,000
Accounting fees and expenses	$	75,000
Printing, transfer agent fees and miscellaneous expenses	$	13,000
Total	$	413,463

Item 14. Indemnification of Directors and Officers.

Section 145(a) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party to or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses that the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the DGCL provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the DGCL.

Additionally, our Charter limits our directors’ and officers’ liability to the fullest extent permitted under the DGCL. The DGCL provides that directors and officers of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors or officers, except for liability:

- for any transaction from which the director or officer derives an improper personal benefit;
- for any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

- for a director under Section 174 of the DGCL;
- for any breach of a duty of loyalty to the corporation or its stockholders; or
- for an officer in any action by or in the right of the corporation.

If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors or officers, then the liability of the Company's directors and officers will be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Delaware law and our Bylaws provide that Orchestra will, in certain situations, indemnify its directors and officers and may indemnify other employees and other agents, to the fullest extent permitted by law. Any indemnified person is also entitled, subject to certain limitations, to advancement, direct payment, or reimbursement of reasonable expenses (including attorneys' fees and disbursements) in advance of the final disposition of the proceeding.

In addition, we have entered into separate indemnification agreements with our directors and officers. These agreements, among other things, require us to indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of their services as one of our directors or officers or any other company or enterprise to which the person provides services at our request.

We maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers.

Item 15. Recent Sales of Unregistered Securities.

The following sets forth information as to all of the Registrant's securities sold in the last three years which were not registered under the Securities Act. Capitalized terms used and not defined in this Item 15 have the meaning given to them in the prospectus which forms a part of this registration statement.

The Registrant issued the following securities in transactions not involving an underwriter and not requiring registration under Section 5 of the Securities Act in reliance on the exemption afforded by Section 4(a)(2) thereof.

Backstop Agreement

Simultaneously with the execution of the Merger Agreement and Forward Purchase Agreements, HSAC2, Orchestra and the RTW Funds entered into the Backstop Agreement, pursuant to which the RTW Funds, jointly and severally, agreed to purchase such number of HSAC2 Ordinary Shares at a price of $10.00 per share to the extent that the amount of cash remaining in HSAC2's working capital and trust account as of immediately prior to the closing of the Merger is less than $60.0 million (which calculation excludes amounts received pursuant to Medtronic's Forward Purchase Agreement or are otherwise held in the HSAC2 Trust Account in respect of Medtronic's Forward Purchase Shares, but is inclusive of amounts received pursuant to the RTW Funds' Forward Purchase Agreement and otherwise held in the HSAC2 Trust Account in respect of the RTW Funds' Forward Purchase Shares).

Pursuant to the Backstop Agreement, the RTW Funds purchased 1,808,512 HSAC2 Ordinary Shares on January 25, 2023, immediately prior to the Domestication.

Officer and Director Warrants

Pursuant to the terms of the Merger Agreement, immediately following the Sponsor Forfeiture and prior to the closing of the Business Combination, HSAC2 issued 750,000 Officer and Director Warrants to purchase shares of our Common Stock to eleven specified employees and directors of Legacy Orchestra for no consideration.

Warrants Issued to Avenue

In connection with the repayment and termination of the 2022 Loan and Security Agreement, on October 6, 2023, the Company issued two warrants to purchase an aggregate of 27,707 shares of Common Stock to Avenue at an exercise price of $7.67 per share. The warrants were issued in lieu of a cash payment of $212,500 due with respect to certain fees under the 2022 Loan and Security Agreement.

Item 16. Exhibits and Financial Statement Schedules.

The following exhibits are filed as part of this registration statement:

Exhibit	Description
2.1#	Agreement and Plan of Merger dated as of July 4, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc. (incorporated by reference to Annex A-1 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
2.2#	Amendment No. 1 to Agreement and Plan of Merger dated as of July 21, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc.((incorporated by reference to Annex A-2 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
2.3#	Amendment No. 2 to Agreement and Plan of Merger dated as of November 21, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc. (incorporated by reference to Annex A-3 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
3.1	Certificate of Incorporation of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
3.2	Bylaws of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
4.1	Form of Common Stock Warrant, issued by Orchestra BioMed, Inc. in the Formation Mergers in exchange for Caliber, BackBeat and FreeHold warrants (incorporated by reference to Exhibit 4.4 of HSAC2's Form S-4 (File No. 333-266660)).
4.2	Form of Amendment to Common Stock Warrant, issued by Orchestra BioMed, Inc. in the Formation Mergers in exchange for Caliber, BackBeat and FreeHold warrants (incorporated by reference to Exhibit 4.5 of HSAC2's Form S-4 (File No. 333-266660)).
4.3	Form of Amended and Restated Common Stock Warrant, issued by Orchestra BioMed, Inc. to designees of Aegis Capital Corp. (incorporated by reference to Exhibit 4.6 of HSAC2's Form S-4 (File No. 333-266660)).
4.4	Form of Special Advisory Common Stock Warrant, issued by Orchestra BioMed, Inc. to its strategic advisers, dated May 31, 2018 (incorporated by reference to Exhibit 4.7 of HSAC2's Form S-4 (File No. 333-266660)).
4.5	Form of Amendment to Special Advisory Common Stock Warrant, issued by Orchestra BioMed, Inc. to its strategic advisers (incorporated by reference to Exhibit 4.8 of HSAC2's Form S-4 (File No. 333-266660)).
4.6	Form of Common Stock Warrant, issued by Orchestra BioMed, Inc. to SLD Capital Corp., dated August 13, 2018 (incorporated by reference to Exhibit 4.9 of HSAC2's Form S-4 (File No. 333-266660)).
4.7	Form of Amendment to Common Stock Warrant, issued by Orchestra BioMed, Inc. to SLD Capital Corp. (incorporated by reference to Exhibit 4.10 of HSAC2's Form S-4 (File No. 333-266660)).
4.8	Investors' Rights Agreement, by and among Orchestra BioMed, Inc. and the investors listed on Schedule A thereto, dated May 31, 2018 (incorporated by reference to Exhibit 4.11 of HSAC2's Form S-4 (File No. 333-266660)).
4.9	Form of Subscription Agreement for shares of Orchestra BioMed, Inc. Series B-1 Preferred Stock (incorporated by reference to Exhibit 4.12 of HSAC2's Form S-4 (File No. 333-266660)).
4.10	Common Stock Warrant, issued by Orchestra BioMed, Inc. to Avenue Venture Opportunities Fund, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 4.14 of HSAC2's Form S-4 (File No. 333-266660)).
4.11	Common Stock Warrant, issued by Orchestra BioMed, Inc. to Avenue Venture Opportunities Fund II, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 4.15 of HSAC2's Form S-4 (File No. 333-266660)).
4.12	Form of Officer and Director Warrant issued pursuant to the Merger Agreement (incorporated by reference to Exhibit 4.16 of HSAC2's Form S-4 (File No. 333-266660)).
4.13	Amended & Restated Warrant issued to HSAC 2 Holdings, LLC, dated January 25, 2023 (incorporated by reference to Exhibit 4.14 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
4.14+	Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund, L.P., dated October 6, 2023.
4.15+	Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund II, L.P., dated October 6, 2023.

Exhibit	Description
5.1+	Opinion of Paul Hastings LLP.
10.1	Amended and Restated Registration Rights and Lock-Up Agreement, dated January 26, 2023, by and among Health Sciences Acquisitions Corporation 2, equityholders thereof and certain stockholders of Orchestra BioMed, Inc. (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.2*	Form of Indemnification Agreement of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.3	Amended and Restated Parent Support Agreement dated as of November 21, 2022 by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., HSAC 2 Holdings, LLC, Alice Lee, Stephanie A. Sirota, Pedro Granadillo, Stuart Peltz, Michael Brophy, and Carsten Boess (incorporated by reference to Exhibit 10.16 of HSAC2's Form S-4 (File No. 333-266660)).
10.4	Orchestra Support Agreement dated as of July 4, 2022 by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., and Covidien Group S.À.R.L. (incorporated by reference to Exhibit 10.5 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.5	Form of Earnout Election Agreement, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc. and the securityholders thereto (incorporated by reference to Exhibit 10.7 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.6*	Orchestra BioMed, Inc. 2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.19 of HSAC2's Form S-4 (File No. 333-266660).
10.7*	Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.8*	Form of Stock Option Grant Notice and Stock Option Agreement under the Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.8 to the Current Report on Form 8- K filed with the SEC on January 31, 2023).
10.9*	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.10^	Commercial Lease, by and between Caliber Therapeutics, Inc. and Union Square, L.P. for facilities at 150 and 140 Union Square Drive, New Hope, Pennsylvania, dated December 14, 2009 and amended June 22, 2010, February 1, 2011, September 18, 2012, January 15, 2015, January 20, 2017, August 8, 2017, and January 29, 2019 (incorporated by reference to Exhibit 10.23 of HSAC2's Form S-4 (File No. 333-266660)).
10.11	Agreement of Lease, by and between Orchestra BioMed, Inc. and ESRT One Grand Central Place, L.L.C. for facilities at Room/Suite 2430, One Grand Central Place, 60 East 42nd Street, New York, New York, dated November 5, 2019 (incorporated by reference to Exhibit 10.24 of HSAC2's Form S-4 (File No. 333-266660)).
10.12	Irrevocable Standby Letter of Credit, issued by Silicon Valley Bank to Orchestra BioMed, Inc. for the benefit of ERST One Grand Central Place, L.L.C., dated October 28, 2019 and amended September 20, 2022 (incorporated by reference to Exhibit 10.25 of HSAC2's Form S-4 (File No. 333-266660)).
10.13	License Agreement, by and between MOTUS GI Holdings, Inc. and Orchestra BioMed, Inc. for facilities at Suite 310, 1301 East Broward Boulevard, Fort Lauderdale, Florida, dated January 22, 2020 (incorporated by reference to Exhibit 10.26 of HSAC2's Form S-4 (File No. 333-266660)).
10.14	Amendment to License Agreement, by and between MOTUS GI Holdings, Inc. and Orchestra BioMed, Inc., dated May 1, 2022 (incorporated by reference to Exhibit 10.27 of HSAC2's Form S-4 (File No. 333-266660)).
10.15^	Exclusive License and Collaboration Agreement, by and among Orchestra BioMed, Inc., BackBeat Medical, LLC, and Medtronic, Inc. dated June 30, 2022 (incorporated by reference to Exhibit 10.28 of HSAC2's Form S-4 (File No. 333-266660)).
10.16^	Distribution Agreement, by and among Orchestra BioMed, Inc., Terumo Corporation and Terumo Medical Corporation, dated June 13, 2019 (incorporated by reference to Exhibit 10.29 of HSAC2's Form S-4 (File No. 333-266660)).
10.17	Loan and Security Agreement, by and among Orchestra BioMed, Inc., Avenue Venture Opportunities Fund II, L.P., and Avenue Venture Opportunities Fund II, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 10.30 of HSAC2's Form S-4 (File No. 333-266660)).
10.18	Stock Purchase Agreement, by and among Orchestra BioMed, Inc., Orchestra Medical Ventures, LLC and Accelerated Technologies, Inc., dated December 20, 2019 (incorporated by reference to Exhibit 10.31 of HSAC2's Form S-4 (File No. 333-266660)).

Exhibit	Description
10.19*#	Employment Agreement, by and between Orchestra BioMed Holdings, Inc. and David P. Hochman, dated January 26, 2023 (incorporated by reference to Exhibit 10.19 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.20*#	Employment Agreement, by and between Orchestra BioMed Holdings, Inc. and Darren R. Sherman, dated January 26, 2023 (incorporated by reference to Exhibit 10.20 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.21*	Employment Agreement, by and between Orchestra BioMed, Inc. and Yuval Mika, dated May 31, 2018 (incorporated by reference to Exhibit 10.34 of HSAC2's Form S-4 (File No. 333-266660).
10.22*	Offer Letter, by and between Orchestra BioMed, Inc. and Michael D. Kaswan, dated January 9, 2022 (incorporated by reference to Exhibit 10.35 of HSAC2's Form S-4 (File No. 333-266660).
10.23	Forward Purchase Agreement dated as of July 4, 2022, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., and Covidien Group S.a.r.l. (incorporated by reference to Exhibit 10.1 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.24	Forward Purchase Agreement dated as of July 4, 2022, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., and RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd., and RTW Venture Fund Limited (incorporated by reference to Exhibit 10.2 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.25	Amendment No. 1 to Forward Purchase Agreement dated as of October 21, 2022, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., and RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd., and RTW Venture Fund Limited (incorporated by reference to Exhibit 10.1 to HSAC2's Current Report on Form 8-K filed with the SEC on October 21, 2022).
10.26	Backstop Agreement dated as of July 4, 2022, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd., and RTW Venture Fund Limited (incorporated by reference to Exhibit 10.3 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.27	Amendment No. 1 to Backstop Agreement dated as of October 21, 2022, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd., and RTW Venture Fund Limited (incorporated by reference to Exhibit 10.2 to HSAC2's Current Report on Form 8-K filed with the SEC on October 21, 2022).
10.28*	Consulting Agreement, dated as of June 5, 2023, by and between the Company and Michael Kaswan (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on June 8, 2023).
10.29*	Offer Letter, dated as of June 5, 2023, by and between the Company and Andrew Taylor (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on June 8, 2023).
10.30*+	Offer Letter, dated as of June 10, 2021, by and between Orchestra BioMed, Inc and George Papandreou.
10.31*+	Promotion Letter, dated as of January 16, 2023, by and between the Company and George Papandreou.
10.32*+	Offer Letter, dated as of May 24, 2023, by and between the Company and William Little.
21.1	List of Subsidiaries of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 21.1 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
23.1+	Consent of Ernst & Young LLP, independent registered public accounting firm of Orchestra BioMed Holdings, Inc.
23.2+	Consent of Paul Hastings LLP (included in Exhibit 5.1).
24.1+	Power of Attorney (included on the signature page to this Registration Statement).
101.INS+	Inline XBRL Instance Document.
101.SCH+	Inline XBRL Taxonomy Extension Schema Document.
101.CAL+	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF+	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB+	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE+	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
107+	Calculation of Filing Fee Table.

+ Filed herewith.

* Indicates a management contract or compensatory plan.

^ Certain identified information has been omitted pursuant to Item 601(b)(10) of Regulation S-K because such information is both (i) not material and (ii) information that the Registrant treats as private or confidential. The Registrant hereby undertakes to furnish supplemental copies of the unredacted exhibit upon request by the SEC.

Certain of the exhibits and schedules to this Exhibit have been omitted in accordance with Regulation S-K Item 601. The Registrant agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon its request.

Item 17. Undertakings.

The undersigned registrant, hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the “Calculation of Registration Fee” table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

provided, *however*, that: Paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. *Provided*, *however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

Insofar as indemnification for liabilities arising under the Securities may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of New York, State of New York, on the 10th day of October, 2023.

ORCHESTRA BIOMED HOLDINGS, INC.

By: /s/ David P. Hochman
Name: David P. Hochman
Title: Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints each of David P. Hochman and Andrew L. Taylor, acting alone or together with another attorney-in-fact, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and substitution, for such person and in his or her name, place and stead, in any and all capacities, to sign any or all further amendments (including post-effective amendments) to this registration statement (and any additional registration statement related hereto permitted by Rule 426(b) promulgated under the Securities Act (and all further amendments, including post-effective amendments thereto)), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ David P. Hochman David P. Hochman	Chief Executive Officer, Chairperson and Director (*Principal Executive Officer*)	October 10, 2023
/s/ Andrew L. Taylor Andrew L. Taylor	Chief Financial Officer (*Principal Financial Officer*)	October 10, 2023
/s/ Joshua Aiello Joshua Aiello	Corporate Controller (*Principal Accounting Officer*)	October 10, 2023
/s/ Jason Aryeh Jason Aryeh	Director	October 10, 2023
/s/ Pamela A. Connealy Pamela A. Connealy	Director	October 10, 2023
/s/ Eric S. Fain, M.D. Eric S. Fain, M.D.	Director	October 10, 2023
/s/ Eric A. Rose, M.D. Eric A. Rose, M.D.	Director	October 10, 2023
/s/ Darren R. Sherman Darren R. Sherman	President, Chief Operating Officer and Director	October 10, 2023
/s/ Geoffrey W. Smith Geoffrey W. Smith	Director	October 10, 2023

Exhibit 4.14

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE AND DISTRIBUTION THEREOF, AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT") OR ANY STATE SECURITIES LAWS. SUCH SECURITIES MAY NOT BE SOLD OR TRANSFERRED IN THE ABSENCE OF (A) SUCH REGISTRATION, (B) AN OPINION OF COUNSEL IN A FORM REASONABLY ACCEPTABLE TO COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED DUE TO AN EXEMPTION THEREFROM UNDER SAID ACT AND ANY APPLICABLE STATE SECURITIES LAWS, (C) ORCHESTRA BIOMED HOLDINGS, INC. OTHERWISE SATISFIES ITSELF THAT SUCH TRANSACTION IS COMPLIANT WITH SUCH LAWS OR (D) A VALID EXEMPTION FROM SUCH REQUIREMENT AS TO SUCH SECURITIES UNDER THE SECURITIES ACT.

Date of Issuance: October 6, 2023

WARRANT TO PURCHASE

SHARES OF STOCK OF

ORCHESTRA BIOMED

HOLDINGS, INC.

(Void after October 6, 2028)

This certifies that AVENUE VENTURE OPPORTUNITIES FUND, L.P., a Delaware limited partnership, or permitted assigns ("Holder"), for value received, is entitled to purchase from ORCHESTRA BIOMED HOLDINGS, INC., a Delaware corporation ("Company"), the Applicable Number (hereinafter defined) of fully paid and nonassessable shares of the common stock of Company ("Common Stock") (the "Warrant Stock"), for cash, at a purchase price per share equal to the Stock Purchase Price (hereinafter defined). Holder may also exercise this Warrant on a cashless or "net issuance" basis as described in Section 1.2 below, and this Warrant shall be deemed to have been exercised in full on such basis on the Expiration Date (hereinafter defined), to the extent not fully exercised prior to such date. This Warrant is issued in in lieu of certain cash payments owed by the Company's subsidiary, Orchestra BioMed, Inc. ("Orchestra"), to the Lenders (as defined below) in connection with the payoff of that certain Loan and Security Agreement and Supplement thereto, both dated as of June 3, 2023 (as amended, restated and supplemented from time to time, the "Loan Agreement" and the "Supplement", respectively), between Orchestra, as borrower, Holder, as a lender and in its capacity as administrative agent and collateral agent (in such capacity, the "Agent") and AVENUE VENTURE OPPORTUNITIES FUND II, L.P., a Delaware limited partnership (in its capacity as a lender, together with Holder, each a "Lender" and collectively, "Lenders"). Capitalized terms used herein and not otherwise defined in this Warrant shall have the meaning(s) ascribed to them in the Loan Agreement and the Supplement, unless the context would otherwise require.

"Applicable Number" means the number of shares of Warrant Stock purchasable hereunder obtained by dividing (A) $42,500 (such amount sometimes referred to hereinafter as the "Coverage Amount") by (B) $7.67, which is the closing price of the Common Stock on the Nasdaq Global Market on

the trading day immediately preceding issuance of this Warrant (rounded up to the nearest whole number if the Applicable Number results in a fractional share of Warrant Stock).

"Stock Purchase Price" means $7.67, which is the closing price of the Common Stock on the Nasdaq Global Market on the trading day immediately preceding issuance of this Warrant.

This Warrant may be exercised at any time or from time to time up to and including 5:00 p.m. (Pacific time) on October 6, 2028 (the "Expiration Date"), upon surrender to Company at its principal office at 60 East 42nd Street, Suite 2430, New York, NY 10165 (or at such other location as Company may advise Holder in writing) of this Warrant properly endorsed with the Form of Subscription attached hereto duly completed and signed and, unless this Warrant is being exercised pursuant to Section 1.2, upon payment in cash or by check of the aggregate Stock Purchase Price for the number of shares for which this Warrant is being exercised determined in accordance with the provisions hereof. Notwithstanding any contrary provision herein, if this Warrant was originally executed and/or delivered electronically, in no event shall Holder be required to surrender or deliver an ink-signed paper copy of this Warrant in connection with its exercise hereof or of any rights hereunder, nor shall Holder be required to surrender or deliver a paper or other physical copy of (i) this Warrant or (ii) any other document in connection with any exercise hereof.

This Warrant is subject to the following terms and conditions:

1. Exercise; Issuance of Certificates; Payment for Shares.

1.1 Unless an election is made pursuant to Section 1.2, this Warrant shall be exercisable at the option of Holder, at any time or from time to time, on or before the Expiration Date for all or any portion of the shares of Warrant Stock (but not for a fraction of a share) which may be purchased hereunder for the Stock Purchase Price multiplied by the number of shares to be purchased. Company agrees that the shares of Warrant Stock purchased under this Warrant shall be and are deemed to be issued to Holder as the record owner of such shares as of the close of business on the date on which the form of subscription shall have been delivered and payment made for such shares. Subject to the provisions of Section 2, upon any exercise of this Warrant for all or any portion of the Warrant Stock that may be purchased hereunder, Holder shall deliver to Company such documents and instruments as the Board of Directors of Company determine to be necessary or appropriate. Except as provided in Section 1.2, in case of a purchase of less than all the shares which may be purchased under this Warrant, Company shall cancel this Warrant and execute and deliver a new Warrant or Warrants of like tenor for the balance of the shares purchasable under this Warrant surrendered upon such purchase to Holder within a reasonable time.

1.2 Cashless Exercise. Holder, in lieu of exercising this Warrant by the cash payment of the Stock Purchase Price pursuant to Section 1.1, may elect, at any time on or before the Expiration Date, to surrender this Warrant and receive that number of shares of Warrant Stock computed using the following formula:

$$X = \frac{Y(A - B)}{A}$$

Where: X = the number of shares of Warrant Stock to be issued to Holder.

Y = the number of shares of Warrant Stock that Holder would otherwise have been entitled to purchase hereunder pursuant to Section 1.1 (or such lesser number of shares as Holder may designate in the case of a partial exercise of this Warrant).

A = the Fair Market Value (as determined pursuant to Section 1.3, below) of one share of Warrant Stock.

B = the Stock Purchase Price then in effect.

Election to exercise under this Section 1.2 may be made by delivering a signed form of subscription to Company via facsimile or electronic mail, to be followed by delivery of this Warrant. Notwithstanding anything to the contrary contained in this Warrant, if as of the close of business on the last business day preceding the Expiration Date this Warrant remains unexercised as to all or a portion of the shares of Warrant Stock purchasable hereunder, then effective as 9:00 a.m. (Pacific time) on the Expiration Date, Holder shall be deemed, automatically and without need for notice to Company, to have elected to exercise this Warrant in full pursuant to the provisions of this Section 1.2, and upon surrender of this Warrant shall be entitled to receive that number of shares of Warrant Stock computed using the above formula, provided that the application of the formula as of the Expiration Date yields a positive number for "X".

For purposes of Rule 144 ("Rule 144") promulgated under the Securities Act of 1933, as amended (the "Securities Act"), it is acknowledged and agreed that (i) the shares issuable upon any exercise of this Warrant in any cashless exercise transaction shall be deemed to have been acquired on the date of issuance of this Warrant, and (ii) the holding period for any shares issuable upon the exercise of this Warrant in any cashless exercise transaction shall be deemed to have commenced on the date of issuance of this Warrant.

1.3 Fair Market Value. If shares of Warrant Stock are then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "Trading Market"), the fair market value of a share of Warrant Stock (the "Fair Market Value") shall be the closing price or last sale price of a share of such class of stock reported for the business day immediately before the date on which Holder delivers this Warrant, together with a Form of Subscription, to the Company. If shares of Warrant Stock are not then traded in a Trading Market, then the Board of Directors of the Company shall determine the Fair Market Value of a share of Warrant Stock in its reasonable good faith judgment, *provided that* in the case of any dispute by the Holder as to the Board of Directors' determination of Fair Market Value or any dispute in respect of any other computation required to be made hereunder, the parties agree to negotiate any such disputes in good faith.

2. Limitation on Transfer.

2.1 This Warrant and the Warrant Stock shall not be transferable except upon the conditions specified in this Section 2, which conditions are intended to ensure compliance with the provisions of the Securities Act. Each holder of this Warrant or the Warrant Stock issuable hereunder will cause any proposed transferee of the Warrant or Warrant Stock to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Section 2. Notwithstanding the foregoing and any other provision of this Section 2 but subject to the last sentence of Section 2.4, Holder may freely transfer all or part of this Warrant or the shares issuable upon exercise of this Warrant (or the securities issuable, directly or indirectly, upon conversion of the shares, if any) at any time to any affiliate of Holder, by giving Company notice of the portion of the Warrant being transferred setting forth the name, address and taxpayer identification number of the transferee and surrendering this Warrant to Company for reissuance to the transferees(s) (and Holder, if applicable). Notwithstanding anything herein to the contrary, Holder may not, without the Company's prior written consent, transfer this Warrant or any portion thereof, or any shares of Warrant Stock issued upon any exercise hereof, to any person or entity who directly competes with the Company, except in connection with an acquisition of the Company by such direct competitor approved by the Company's board of directors.

2.2 Except as provided in Section 2.3 or unless such securities have been sold pursuant to Rule 144 or pursuant to an effective registration statement under the Securities Act, each certificate representing (i) this Warrant, (ii) the Warrant Stock and (iii) any other securities issued in respect to Common Stock issued upon any stock split, stock dividend, recapitalization, merger, consolidation or

similar event, shall be stamped or otherwise imprinted with a legend substantially in the following form (in addition to any legend required under applicable state securities laws):

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE AND DISTRIBUTION THEREOF, AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OR ANY STATE SECURITIES LAWS. SUCH SECURITIES MAY NOT BE SOLD OR TRANSFERRED IN THE ABSENCE OF (A) SUCH REGISTRATION, (B) AN OPINION OF COUNSEL IN A FORM REASONABLY ACCEPTABLE TO COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED DUE TO AN EXEMPTION THEREFROM UNDER SAID ACT AND ANY APPLICABLE STATE SECURITIES LAWS OR (C) ORCHESTRA BIOMED HOLDINGS, INC. OTHERWISE SATISFIES ITSELF THAT SUCH TRANSACTION IS COMPLIANT WITH SUCH LAWS.

2.3 Holder acknowledges that the Company is an issuer described in subparagraph (i)(1)(ii) of Rule 144. Any Warrant Stock issued pursuant to this Warrant shall initially be issued in Holder's name (or its designee's name) in book entry form on the records of the Company's transfer agent (the "Transfer Agent"), and, other than in connection with a sale either registered under the Securities Act or made pursuant Rule 144, will not be permitted to be transferred to a Holder's own brokerage account for a period of at least one year from (i) the date of issuance of the Warrant Stock or (ii) the date of issuance of this Warrant if the Warrant Stock is issued pursuant to Section 1.2) (as applicable, the "One Year Period") and then only if an opinion is provided that is acceptable to the Transfer Agent with respect to removal of the restricted legend on the Warrant Stock (a "Legend Removal Opinion"). In connection with a Legend Removal Opinion, Holder shall, if requested by the Company, provide certain representations regarding only making sales when there is current public information regarding the Company, as required by subparagraph (i)(2) of Rule 144. If requested by Holder, after the expiration of the One-Year Period, the Company shall use its commercially reasonable efforts to cause its counsel to issue a Legend Removal Opinon and permit the transfer of Warrant Stock to Holder's brokerage account.

2.4 Holder of this Warrant and each person to whom this Warrant is subsequently transferred represents and warrants to Company and agrees (by acceptance of such transfer) that it will not transfer this Warrant (or securities issuable upon exercise hereof unless a registration statement under the Securities Act was in effect with respect to the issuance of such securities) unless (i) pursuant to an effective registration statement under the Securities Act and applicable state securities laws covering any such transaction, (ii) pursuant to Rule 144 (or any successor rule under the Securities Act permitting the public disposition of securities), (iii) Company receives an opinion of counsel, reasonably satisfactory to Company, that an exemption from such registration is available or (iv) Company otherwise satisfies itself that such transaction is exempt from registration.

3. Shares to be Fully Paid; Reservation of Shares. Company covenants and agrees that all shares of Warrant Stock which may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be duly authorized, validly issued, fully paid and nonassessable and free from all preemptive rights of any stockholder and free of all taxes, liens and charges with respect to the issue thereof. Company further covenants and agrees that during the period within which the rights represented by this Warrant may be exercised, Company will at all times have authorized and reserved, for the purpose of issue or transfer upon exercise of the subscription rights evidenced by this Warrant, a sufficient number of shares of authorized but unissued Warrant Stock, or other securities and property, when and as required to provide for the exercise of the rights represented by this Warrant. Company will take all such action as may be necessary to assure that such shares of Warrant Stock may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any domestic securities exchange upon which the Warrant Stock may be listed. Company will not take any action which would result in any adjustment of the Stock Purchase Price (i) if the total number of shares of Warrant Stock issuable after such action upon exercise of all outstanding warrants, together with all shares of Warrant Stock then outstanding and

all shares of Warrant Stock then issuable upon exercise of all options and upon the conversion of all convertible securities then outstanding, would exceed the total number of shares of Warrant Stock then authorized by Company's Certificate of Incorporation, as amended and restated from time to time (the "Charter") or (ii) if the par value per share of the Warrant Stock would exceed the Stock Purchase Price.

4. Adjustment to Warrant Stock and Stock Purchase Price.

4.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of Warrant Stock payable in additional shares of Warrant Stock or other securities or property (other than cash), then upon exercise of this Warrant, for each share of Warrant Stock acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the shares of Warrant Stock of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of Warrant Stock by reclassification or otherwise into a greater number of shares, the number of shares of Warrant Stock purchasable hereunder shall be proportionately increased and the Stock Purchase Price shall be proportionately decreased. If the outstanding shares of Warrant Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Stock Purchase Price shall be proportionately increased and the number of shares of Warrant Stock shall be proportionately decreased.

4.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of Warrant Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the shares of Warrant Stock been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 4.2 shall similarly apply to successive reclassifications, exchanges, combinations, substitutions, replacements or other similar events.

4.3 Notice/Certificate as to Adjustments. Upon each adjustment of the Stock Purchase Price, class and/or number of shares issuable upon exercise of this Warrant, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Stock Purchase Price, class and/or number of shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Stock Purchase Price, class and number of shares in effect upon the date of such adjustment.

5. Issue Tax. The issuance of certificates for shares of Warrant Stock upon the exercise of this Warrant shall be made without charge to Holder of this Warrant for any issue tax in respect thereof; provided, however, that Company shall not be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of any certificate in a name other than that of the then Holder of this Warrant being exercised.

6. No Impairment. The Company shall not, by amendment of its Charter or bylaws, amendment of the Rights Agreement, or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities, or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed by it hereunder, but shall at all times in good faith assist in the carrying out of all the provisions of this Warrant.

7. No Voting Rights; Limitation of Liability. Nothing contained in this Warrant shall be construed as conferring upon Holder hereof the right to vote or to consent as a stockholder in respect of meetings of stockholders for the election of directors of Company or any other matters or any rights whatsoever as a stockholder of Company. No dividends or interest shall be payable in respect of this

Warrant or the interest represented hereby or the shares purchasable hereunder until, and only to the extent that, this Warrant shall have been exercised; provided, however, that if any dividends are due or paid at any time on the underlying securities for which this Warrant is exercisable, then upon exercise, the securities issued to Holder shall be deemed to have accrued dividends and be paid identical dividends from the same time as the outstanding shares for which this Warrant is exercisable were first issued (or, if later, the date of this Warrant). No provisions hereof, in the absence of affirmative action by Holder to purchase shares of Warrant Stock, and no mere enumeration herein of the rights or privileges of Holder hereof, shall give rise to any liability of such Holder for the Stock Purchase Price or as a stockholder of Company, whether such liability is asserted by Company or by its creditors.

8. Amendment of Charter. Unless Holder consents thereto in writing, Company shall not amend its Charter prior to the exercise of this Warrant if the Warrant Stock would be adversely affected by such amendment in a manner that would be more adverse to Holder with respect to the shares of Warrant Stock issuable upon the exercise of this Warrant than, and substantially disproportionate to, such amendment's effect on the other holders of the same class or series of Warrant Stock.

9. Registration Rights. The Company shall register the resale of the Warrant Stock issuable upon exercise of this Warrant under the Securities Act on Form S-1 (or any other form available to the Company at the time) within ninety (90) days of the date of issuance of this Warrant and shall maintain such registration for as long as the Company is required to maintain the registration of "Registrable Securities" (as such term in defined in the Company's Amended and Restated Registration Rights and Lock-Up Agreement, dated January 26, 2023 (the "Company RRA")) pursuant to the Company RRA. For the avoidance of doubt, the Company shall comply with the provisions of Article III (Company Procedures) and Article V (Indemnification and Contribution) of the Company RRA in connection with the registration of the resale of any Warrant Stock issuable upon exercise of this Warrant.

10. Rights and Obligations Survive Exercise of Warrant. The rights and obligations of Company, of Holder of this Warrant and of the holder of shares of Warrant Stock issued upon exercise of this Warrant, contained in Sections 2, 6, 8, 9 and 18 shall survive the exercise of this Warrant.

11. Modification and Waiver. This Warrant and any provision hereof may be changed, waived, discharged or terminated only by an instrument in writing signed by the party against which enforcement of the same is sought.

12. Notices. Any notice, request or other document required or permitted to be given or delivered to Holder or Company shall be deemed to have been given (i) upon receipt if delivered personally, (ii) upon confirmation of receipt if by electronic mail or telecopy (or, if no confirmation is received, then on the next business day), (iii) one business day after the business day of deposit with a nationally recognized overnight courier, specifying next-day delivery, with written verification of receipt, or (iv) three business days after deposit in the US mail, with postage prepaid and certified or registered, to each such Holder at its address as shown on the books of Company or to Company at the address indicated therefor in the opening paragraphs of this Warrant (or at such other location as Company advises Holder in writing).

13. Survival of Certain Obligations. All of the obligations of Company relating to the Warrant Stock issuable upon the exercise of this Warrant shall survive the exercise and termination of this Warrant. All of the covenants and agreements of Company shall inure to the benefit of and be binding upon the successors and permitted assigns of Holder.

14. Descriptive Headings and Governing Law. The descriptive headings of the several sections and paragraphs of this Warrant are inserted for convenience only and do not constitute a part of this Warrant. This Warrant shall be construed and enforced in accordance with, and the rights of the parties shall be governed by, the laws of the State of New York, without giving effect to conflicts of law principles.

15. Lost Warrants or Stock Certificates. Company agrees that upon receipt of evidence reasonably satisfactory to Company of the loss, theft, destruction, or mutilation of any Warrant or stock certificate and, in the case of any such loss, theft or destruction, upon receipt of an indemnity reasonably satisfactory to Company, or in the case of any such mutilation upon surrender and cancellation of such Warrant or stock certificate, Company at its expense will make and deliver a new Warrant or stock certificate, of like tenor, in lieu of the lost, stolen, destroyed or mutilated Warrant or stock certificate.

16. Fractional Shares. No fractional shares shall be issued upon exercise of this Warrant. Company shall, in lieu of issuing any fractional share, pay the holder entitled to such fraction a sum in cash equal to such fraction multiplied by the then effective Stock Purchase Price.

17. Representations of Holder. With respect to this Warrant, Holder represents and warrants to Company as follows:

17.1 Experience. It is experienced in evaluating and investing in companies engaged in businesses similar to that of Company; it understands that investment in this Warrant involves substantial risks; it has made detailed inquiries concerning Company, its business and services, its officers and its personnel; the officers of Company have made available to Holder any and all written information it has requested; the officers of Company have answered to Holder’s satisfaction all inquiries made by it; and it has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risks of investment in Company and it is able to bear the economic risk of that investment.

17.2 Investment. It is acquiring this Warrant for investment for its own account and not with a view to, or for resale in connection with, any distribution thereof. It understands that this Warrant, the shares of Warrant Stock issuable upon exercise thereof have not been registered under the Securities Act, nor qualified under applicable state securities laws. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the shares of Warrant Stock.

17.3 Rule 144. It acknowledges that this Warrant and the Warrant Stock must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. It has been advised or is aware of the provisions of Rule 144 promulgated under the Securities Act.

17.4 Access to Data. It has had an opportunity to discuss Company’s business, management and financial affairs with Company’s management and has had the opportunity to inspect Company’s facilities. Holder is aware of the Company’s business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities, including access to the Company’s filings made pursuant to Section 13 of the Securities Exchange Act of 1934, as amended, on the United States Securities and Exchange Commission’s Electronic Data Gathering, Analysis, and Retrieval System (“EDGAR”). Holder further has had the opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

17.5 Accredited Investor. It is an “accredited investor” within the meaning of Regulation D promulgated under the Securities Act.

18. Additional Representations and Covenants of Company. Company hereby represents, warrants and agrees as follows:

18.1 Corporate Power. Company has all requisite corporate power and corporate authority to issue this Warrant and to carry out and perform its obligations hereunder.

18.2 Authorization. All corporate action on the part of Company, its directors and stockholders necessary for the authorization, execution, delivery and performance by Company of this Warrant has been taken. This Warrant is a valid and binding obligation of Company, enforceable in accordance with its terms except as enforceability may be limited by bankruptcy, insolvency, fraudulent conveyance, reorganization or moratorium laws, other similar laws affecting creditors' rights and general principles of equity affecting the availability of specific performance and other equitable remedies.

18.3 Offering. Subject in part to the truth and accuracy of Holder's representations set forth in Section 17 hereof, the offer, issuance and sale of this Warrant is, and the issuance of Warrant Stock upon exercise of this Warrant will be exempt from the registration requirements of the Securities Act, and are exempt from the qualification requirements of any applicable state securities laws; and neither Company nor anyone acting on its behalf will take any action hereafter that would cause the loss of such exemptions.

18.4 Listing; Stock Issuance. Company shall secure and maintain the listing of the Warrant Stock issuable upon exercise of this Warrant upon each securities exchange or over-the-counter market upon which securities of the same class or series issued by Company are listed, if any. Upon exercise of this Warrant, Company will use commercially reasonable efforts to cause stock certificates representing the shares of Warrant Stock purchased pursuant to the exercise to be issued in the names of Holder, its nominees or assignees, as appropriate at the time of such exercise.

18.5 Charter Documents. Company has filed on EDGAR true and complete copies of Company's Charter, bylaws, each as amended and in effect on the date of issuance of this Warrant.

19. Counterparts; Facsimile; Electronic Mail. Each party's execution and delivery of such party's counterpart signature page to this Warrant via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, e.g., www.docusign.com) shall constitute such party's effective execution and delivery of this Warrant and agreement to and acceptance of the terms hereof for all purposes.

20. Acquisition; Replacement Warrant. In the event of either (i) an Acquisition (as defined below) of the Company, (ii) the consummation of a business combination transaction involving the Company and/or any direct or indirect parent company thereof and a publicly traded U.S. domestic special purpose acquisition company or other similar U.S. domestic corporation that is a "blank check" company under applicable U.S. securities laws and formed for the purpose of effecting such a transaction, or (iii) the consummation of a business combination transaction involving the Company and/or any direct or indirect parent company thereof with any public company listed on a U.S. securities exchange, then in the event this Warrant has not been previously exercised the Company shall cause to be issued to the Holder a replacement warrant exercisable for an equivalent number of shares of common stock of the resulting entity equal to the unexercised portion of this Warrant (the "Replacement Warrant"). The Replacement Warrant shall otherwise contain terms and conditions substantially equivalent to this Warrant. For the purpose of this Warrant, "Acquisition" means any transaction or series of related transactions involving: (A) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company; (B) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (C) any sale or other transfer by the stockholders of the Company of shares representing

at least a majority of the Company's then-total outstanding combined voting power.

21 Notice of Certain Events. If the Company proposes at any time to:

21.1 declare any dividend or distribution upon the outstanding shares of Warrant Stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

21.2 offer for subscription or sale *pro rata* to all holders of the outstanding shares of shares of Warrant Stock any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

21.3 effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of Warrant Stock; or

21.4 effect an Acquisition or to liquidate, dissolve or wind up.

then, in connection with each such event, the Company shall give Holder:

21.5 in the case of the matters referred to in (21.1) and (21.2) above, at least ten (10) business days prior written notice of the earlier to occur of the effective date thereof or the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding Common Stock will be entitled thereto) or for determining rights to vote, if any; and

21.6 in the case of the matters referred to in (21.3) and (21.4) above at least ten (10) business days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of Common Stock will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event and such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such event giving rise to the notice).

provided, that the Company's failure to give any such notice of such actions pursuant to this Section 21 shall not affect the validity of any such actions by the Company.

[*Remainder of this page intentionally left blank; signature page follows*]

IN WITNESS WHEREOF, Company has caused this Warrant to be duly executed by its officer, thereunto duly authorized as of the date of issuance set forth on the first page hereof.

By: /s/ Andrew Taylor
Name: Andrew Taylor
Title: Chief Financial Officer

AGREED AND ACCEPTED:

HOLDER:

AVENUE VENTURE OPPORTUNITIES FUND, L.P.

By: Avenue Venture Opportunities Partners, LLC
Its: General Partner
By: GL Venture Opportunities Partners I LLC
Its: Managing Member

By: /s/ Sonia Gardner
Name: Sonia Gardner
Title: Member

FORM OF SUBSCRIPTION

(To be signed only upon exercise of Warrant)

To: ______________________________

☐ The undersigned, the holder of the within Warrant, hereby irrevocably elects to exercise the purchase right represented by such Warrant for, and to purchase thereunder, (1) ______________ (________) shares[1] (the "Shares") of Stock of __________ and herewith makes payment of ____________________ Dollars ($________) therefor, and requests that the certificates for such shares be issued in the name of, and delivered to,_________, whose address is _________.

☐ The undersigned hereby elects to convert ________ percent (___%) of the value of the Warrant pursuant to the provisions of Section 1.2 of the Warrant.

The undersigned acknowledges that it has reviewed the representations and warranties contained in Section 17 of this Warrant and by its signature below hereby makes such representations and warranties to Company.

Dated ________________

Holder: ________________

By: ________________

Its: ________________

(Address)

____

____

[1] Insert here the number of shares called for on the face of the Warrant (or, in the case of a partial exercise, the portion thereof as to which the Warrant is being exercised), in either case without making any adjustment for additional Warrant Stock or any other stock or other securities or property or cash which, pursuant to the adjustment provisions of the Warrant, may be issuable upon exercise.

ASSIGNMENT

FOR VALUE RECEIVED, the undersigned, the holder of the within Warrant, hereby sells, assigns and transfers all of the rights of the undersigned under the within Warrant, with respect to the number of shares of Warrant Stock covered thereby set forth herein below, unto:

Name of Assignee	Address	No. of Shares

Dated ____________________

Holder: ____________________

By: ____________________

Its: ____________________

EXHIBIT "A"

[On letterhead of Company]

Reference is hereby made to that certain Warrant dated October 6, 2023 issued by ORCHESTRA BIOMED HOLDINGS, INC., a Delaware corporation (the "Company"), to AVENUE VENTURE OPPORTUNITIES FUND, L.P., a Delaware limited partnership (the "Holder").

[IF APPLICABLE] The Warrant provides that the actual number and type of shares of Company's capital stock issuable upon exercise of the Warrant and the initial exercise price per share are to be determined by reference to one or more events or conditions subsequent to the issuance of the Warrant. Such events or conditions have now occurred or lapsed, and Company wishes to confirm the actual number of shares issuable and the initial exercise price. The provisions of this Supplement to Warrant are incorporated into the Warrant by this reference, and shall control the interpretation and exercise of the Warrant.

This certifies that Holder is entitled to purchase from Company ___________, at the Holder's option, either (i) (________) fully paid and nonassessable shares of Company's ______ Stock at a price of _______ Dollars ($_________) per share or (ii) (   ) fully paid and nonassessable shares of Company's _________ Stock at a price of _______ Dollars ($_______) per share.

Executed this _______ day of __________________________, 20________.

ORCHESTRA BIOMED HOLDINGS, INC.

By: ____________________________________

Name: ____________________________________

Title: ____________________________

Exhibit 4.15

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE AND DISTRIBUTION THEREOF, AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT") OR ANY STATE SECURITIES LAWS. SUCH SECURITIES MAY NOT BE SOLD OR TRANSFERRED IN THE ABSENCE OF (A) SUCH REGISTRATION, (B) AN OPINION OF COUNSEL IN A FORM REASONABLY ACCEPTABLE TO COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED DUE TO AN EXEMPTION THEREFROM UNDER SAID ACT AND ANY APPLICABLE STATE SECURITIES LAWS, (C) ORCHESTRA BIOMED HOLDINGS, INC. OTHERWISE SATISFIES ITSELF THAT SUCH TRANSACTION IS COMPLIANT WITH SUCH LAWS OR (D) A VALID EXEMPTION FROM SUCH REQUIREMENT AS TO SUCH SECURITIES UNDER THE SECURITIES ACT.

Date of Issuance: October 6, 2023

WARRANT TO PURCHASE

SHARES OF STOCK OF

ORCHESTRA BIOMED

HOLDINGS, INC.

(Void after October 6, 2028)

This certifies that AVENUE VENTURE OPPORTUNITIES FUND II, L.P., a Delaware limited partnership, or permitted assigns ("Holder"), for value received, is entitled to purchase from ORCHESTRA BIOMED HOLDINGS, INC., a Delaware corporation ("Company"), the Applicable Number (hereinafter defined) of fully paid and nonassessable shares of the common stock of Company ("Common Stock") (the "Warrant Stock"), for cash, at a purchase price per share equal to the Stock Purchase Price (hereinafter defined). Holder may also exercise this Warrant on a cashless or "net issuance" basis as described in Section 1.2 below, and this Warrant shall be deemed to have been exercised in full on such basis on the Expiration Date (hereinafter defined), to the extent not fully exercised prior to such date. This Warrant is issued in in lieu of certain cash payments owed by the Company's subsidiary, Orchestra BioMed, Inc. ("Orchestra"), to the Lenders (as defined below) in connection with the payoff of that certain Loan and Security Agreement and Supplement thereto, both dated as of June 3, 2023 (as amended, restated and supplemented from time to time, the "Loan Agreement" and the "Supplement", respectively), between Orchestra, as borrower, Holder, as a lender and AVENUE VENTURE OPPORTUNITIES FUND, L.P., a Delaware limited partnership (in its capacity as a lender and in its capacity as administrative agent and collateral agent (in such capacity, the "Agent" and, together with Holder, each a "Lender" and collectively, "Lenders"). Capitalized terms used herein and not otherwise defined in this Warrant shall have the meaning(s) ascribed to them in the Loan Agreement and the Supplement, unless the context would otherwise require.

"Applicable Number" means the number of shares of Warrant Stock purchasable hereunder obtained by dividing (A) $170,000 (such amount sometimes referred to hereinafter as the "Coverage Amount") by (B) $7.67, which is the closing price of the Common Stock on the Nasdaq Global Market on

the trading day immediately preceding issuance of this Warrant (rounded up to the nearest whole number if the Applicable Number results in a fractional share of Warrant Stock).

"Stock Purchase Price" means $7.67, which is the closing price of the Common Stock on the Nasdaq Global Market on the trading day immediately preceding issuance of this Warrant.

This Warrant may be exercised at any time or from time to time up to and including 5:00 p.m. (Pacific time) on October 6, 2028 (the "Expiration Date"), upon surrender to Company at its principal office at 60 East 42nd Street, Suite 2430, New York, NY 10165 (or at such other location as Company may advise Holder in writing) of this Warrant properly endorsed with the Form of Subscription attached hereto duly completed and signed and, unless this Warrant is being exercised pursuant to Section 1.2, upon payment in cash or by check of the aggregate Stock Purchase Price for the number of shares for which this Warrant is being exercised determined in accordance with the provisions hereof. Notwithstanding any contrary provision herein, if this Warrant was originally executed and/or delivered electronically, in no event shall Holder be required to surrender or deliver an ink-signed paper copy of this Warrant in connection with its exercise hereof or of any rights hereunder, nor shall Holder be required to surrender or deliver a paper or other physical copy of (i) this Warrant or (ii) any other document in connection with any exercise hereof.

This Warrant is subject to the following terms and conditions:

1. Exercise; Issuance of Certificates; Payment for Shares.

1.1 Unless an election is made pursuant to Section 1.2, this Warrant shall be exercisable at the option of Holder, at any time or from time to time, on or before the Expiration Date for all or any portion of the shares of Warrant Stock (but not for a fraction of a share) which may be purchased hereunder for the Stock Purchase Price multiplied by the number of shares to be purchased. Company agrees that the shares of Warrant Stock purchased under this Warrant shall be and are deemed to be issued to Holder as the record owner of such shares as of the close of business on the date on which the form of subscription shall have been delivered and payment made for such shares. Subject to the provisions of Section 2, upon any exercise of this Warrant for all or any portion of the Warrant Stock that may be purchased hereunder, Holder shall deliver to Company such documents and instruments as the Board of Directors of Company determine to be necessary or appropriate. Except as provided in Section 1.2, in case of a purchase of less than all the shares which may be purchased under this Warrant, Company shall cancel this Warrant and execute and deliver a new Warrant or Warrants of like tenor for the balance of the shares purchasable under this Warrant surrendered upon such purchase to Holder within a reasonable time.

1.2 Cashless Exercise. Holder, in lieu of exercising this Warrant by the cash payment of the Stock Purchase Price pursuant to Section 1.1, may elect, at any time on or before the Expiration Date, to surrender this Warrant and receive that number of shares of Warrant Stock computed using the following formula:

$$X = \frac{Y(A - B)}{A}$$

Where: X = the number of shares of Warrant Stock to be issued to Holder.

Y = the number of shares of Warrant Stock that Holder would otherwise have been entitled to purchase hereunder pursuant to Section 1.1 (or such lesser number of shares as Holder may designate in the case of a partial exercise of this Warrant).

A = the Fair Market Value (as determined pursuant to Section 1.3, below) of one share of Warrant Stock.

B = the Stock Purchase Price then in effect.

Election to exercise under this Section 1.2 may be made by delivering a signed form of subscription to Company via facsimile or electronic mail, to be followed by delivery of this Warrant. Notwithstanding anything to the contrary contained in this Warrant, if as of the close of business on the last business day preceding the Expiration Date this Warrant remains unexercised as to all or a portion of the shares of Warrant Stock purchasable hereunder, then effective as 9:00 a.m. (Pacific time) on the Expiration Date, Holder shall be deemed, automatically and without need for notice to Company, to have elected to exercise this Warrant in full pursuant to the provisions of this Section 1.2, and upon surrender of this Warrant shall be entitled to receive that number of shares of Warrant Stock computed using the above formula, provided that the application of the formula as of the Expiration Date yields a positive number for "X".

For purposes of Rule 144 ("Rule 144") promulgated under the Securities Act of 1933, as amended (the "Securities Act"), it is acknowledged and agreed that (i) the shares issuable upon any exercise of this Warrant in any cashless exercise transaction shall be deemed to have been acquired on the date of issuance of this Warrant, and (ii) the holding period for any shares issuable upon the exercise of this Warrant in any cashless exercise transaction shall be deemed to have commenced on the date of issuance of this Warrant.

1.3 Fair Market Value. If shares of Warrant Stock are then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "Trading Market"), the fair market value of a share of Warrant Stock (the "Fair Market Value") shall be the closing price or last sale price of a share of such class of stock reported for the business day immediately before the date on which Holder delivers this Warrant, together with a Form of Subscription, to the Company. If shares of Warrant Stock are not then traded in a Trading Market, then the Board of Directors of the Company shall determine the Fair Market Value of a share of Warrant Stock in its reasonable good faith judgment, *provided that* in the case of any dispute by the Holder as to the Board of Directors' determination of Fair Market Value or any dispute in respect of any other computation required to be made hereunder, the parties agree to negotiate any such disputes in good faith.

2. Limitation on Transfer.

2.1 This Warrant and the Warrant Stock shall not be transferable except upon the conditions specified in this Section 2, which conditions are intended to ensure compliance with the provisions of the Securities Act. Each holder of this Warrant or the Warrant Stock issuable hereunder will cause any proposed transferee of the Warrant or Warrant Stock to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Section 2. Notwithstanding the foregoing and any other provision of this Section 2 but subject to the last sentence of Section 2.4, Holder may freely transfer all or part of this Warrant or the shares issuable upon exercise of this Warrant (or the securities issuable, directly or indirectly, upon conversion of the shares, if any) at any time to any affiliate of Holder, by giving Company notice of the portion of the Warrant being transferred setting forth the name, address and taxpayer identification number of the transferee and surrendering this Warrant to Company for reissuance to the transferees(s) (and Holder, if applicable). Notwithstanding anything herein to the contrary, Holder may not, without the Company's prior written consent, transfer this Warrant or any portion thereof, or any shares of Warrant Stock issued upon any exercise hereof, to any person or entity who directly competes with the Company, except in connection with an acquisition of the Company by such direct competitor approved by the Company's board of directors.

2.2 Except as provided in Section 2.3 or unless such securities have been sold pursuant to Rule 144 or pursuant to an effective registration statement under the Securities Act, each certificate representing (i) this Warrant, (ii) the Warrant Stock and (iii) any other securities issued in respect to Common Stock issued upon any stock split, stock dividend, recapitalization, merger, consolidation or

similar event, shall be stamped or otherwise imprinted with a legend substantially in the following form (in addition to any legend required under applicable state securities laws):

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE AND DISTRIBUTION THEREOF, AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OR ANY STATE SECURITIES LAWS. SUCH SECURITIES MAY NOT BE SOLD OR TRANSFERRED IN THE ABSENCE OF (A) SUCH REGISTRATION, (B) AN OPINION OF COUNSEL IN A FORM REASONABLY ACCEPTABLE TO COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED DUE TO AN EXEMPTION THEREFROM UNDER SAID ACT AND ANY APPLICABLE STATE SECURITIES LAWS OR (C) ORCHESTRA BIOMED HOLDINGS, INC. OTHERWISE SATISFIES ITSELF THAT SUCH TRANSACTION IS COMPLIANT WITH SUCH LAWS.

2.3 Holder acknowledges that the Company is an issuer described in subparagraph (i)(1)(ii) of Rule 144. Any Warrant Stock issued pursuant to this Warrant shall initially be issued in Holder's name (or its designee's name) in book entry form on the records of the Company's transfer agent (the "Transfer Agent"), and, other than in connection with a sale either registered under the Securities Act or made pursuant Rule 144, will not be permitted to be transferred to a Holder's own brokerage account for a period of at least one year from (i) the date of issuance of the Warrant Stock or (ii) the date of issuance of this Warrant if the Warrant Stock is issued pursuant to Section 1.2) (as applicable, the "One Year Period") and then only if an opinion is provided that is acceptable to the Transfer Agent with respect to removal of the restricted legend on the Warrant Stock (a "Legend Removal Opinion"). In connection with a Legend Removal Opinion, Holder shall, if requested by the Company, provide certain representations regarding only making sales when there is current public information regarding the Company, as required by subparagraph (i)(2) of Rule 144. If requested by Holder, after the expiration of the One-Year Period, the Company shall use its commercially reasonable efforts to cause its counsel to issue a Legend Removal Opinon and permit the transfer of Warrant Stock to Holder's brokerage account.

2.4 Holder of this Warrant and each person to whom this Warrant is subsequently transferred represents and warrants to Company and agrees (by acceptance of such transfer) that it will not transfer this Warrant (or securities issuable upon exercise hereof unless a registration statement under the Securities Act was in effect with respect to the issuance of such securities) unless (i) pursuant to an effective registration statement under the Securities Act and applicable state securities laws covering any such transaction, (ii) pursuant to Rule 144 (or any successor rule under the Securities Act permitting the public disposition of securities), (iii) Company receives an opinion of counsel, reasonably satisfactory to Company, that an exemption from such registration is available or (iv) Company otherwise satisfies itself that such transaction is exempt from registration.

3. Shares to be Fully Paid; Reservation of Shares. Company covenants and agrees that all shares of Warrant Stock which may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be duly authorized, validly issued, fully paid and nonassessable and free from all preemptive rights of any stockholder and free of all taxes, liens and charges with respect to the issue thereof. Company further covenants and agrees that during the period within which the rights represented by this Warrant may be exercised, Company will at all times have authorized and reserved, for the purpose of issue or transfer upon exercise of the subscription rights evidenced by this Warrant, a sufficient number of shares of authorized but unissued Warrant Stock, or other securities and property, when and as required to provide for the exercise of the rights represented by this Warrant. Company will take all such action as may be necessary to assure that such shares of Warrant Stock may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any domestic securities exchange upon which the Warrant Stock may be listed. Company will not take any action which would result in any adjustment of the Stock Purchase Price (i) if the total number of shares of Warrant Stock issuable after such action upon exercise of all outstanding warrants, together with all shares of Warrant Stock then outstanding and

all shares of Warrant Stock then issuable upon exercise of all options and upon the conversion of all convertible securities then outstanding, would exceed the total number of shares of Warrant Stock then authorized by Company's Certificate of Incorporation, as amended and restated from time to time (the "Charter") or (ii) if the par value per share of the Warrant Stock would exceed the Stock Purchase Price.

4. Adjustment to Warrant Stock and Stock Purchase Price.

4.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of Warrant Stock payable in additional shares of Warrant Stock or other securities or property (other than cash), then upon exercise of this Warrant, for each share of Warrant Stock acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the shares of Warrant Stock of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of Warrant Stock by reclassification or otherwise into a greater number of shares, the number of shares of Warrant Stock purchasable hereunder shall be proportionately increased and the Stock Purchase Price shall be proportionately decreased. If the outstanding shares of Warrant Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Stock Purchase Price shall be proportionately increased and the number of shares of Warrant Stock shall be proportionately decreased.

4.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of Warrant Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the shares of Warrant Stock been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 4.2 shall similarly apply to successive reclassifications, exchanges, combinations, substitutions, replacements or other similar events.

4.3 Notice/Certificate as to Adjustments. Upon each adjustment of the Stock Purchase Price, class and/or number of shares issuable upon exercise of this Warrant, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Stock Purchase Price, class and/or number of shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Stock Purchase Price, class and number of shares in effect upon the date of such adjustment.

5. Issue Tax. The issuance of certificates for shares of Warrant Stock upon the exercise of this Warrant shall be made without charge to Holder of this Warrant for any issue tax in respect thereof; provided, however, that Company shall not be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of any certificate in a name other than that of the then Holder of this Warrant being exercised.

6. No Impairment. The Company shall not, by amendment of its Charter or bylaws, amendment of the Rights Agreement, or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities, or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed by it hereunder, but shall at all times in good faith assist in the carrying out of all the provisions of this Warrant.

7. No Voting Rights; Limitation of Liability. Nothing contained in this Warrant shall be construed as conferring upon Holder hereof the right to vote or to consent as a stockholder in respect of meetings of stockholders for the election of directors of Company or any other matters or any rights whatsoever as a stockholder of Company. No dividends or interest shall be payable in respect of this

Warrant or the interest represented hereby or the shares purchasable hereunder until, and only to the extent that, this Warrant shall have been exercised; provided, however, that if any dividends are due or paid at any time on the underlying securities for which this Warrant is exercisable, then upon exercise, the securities issued to Holder shall be deemed to have accrued dividends and be paid identical dividends from the same time as the outstanding shares for which this Warrant is exercisable were first issued (or, if later, the date of this Warrant). No provisions hereof, in the absence of affirmative action by Holder to purchase shares of Warrant Stock, and no mere enumeration herein of the rights or privileges of Holder hereof, shall give rise to any liability of such Holder for the Stock Purchase Price or as a stockholder of Company, whether such liability is asserted by Company or by its creditors.

8. Amendment of Charter. Unless Holder consents thereto in writing, Company shall not amend its Charter prior to the exercise of this Warrant if the Warrant Stock would be adversely affected by such amendment in a manner that would be more adverse to Holder with respect to the shares of Warrant Stock issuable upon the exercise of this Warrant than, and substantially disproportionate to, such amendment's effect on the other holders of the same class or series of Warrant Stock.

9. Registration Rights. The Company shall register the resale of the Warrant Stock issuable upon exercise of this Warrant under the Securities Act on Form S-1 (or any other form available to the Company at the time) within ninety (90) days of the date of issuance of this Warrant and shall maintain such registration for as long as the Company is required to maintain the registration of "Registrable Securities" (as such term in defined in the Company's Amended and Restated Registration Rights and Lock-Up Agreement, dated January 26, 2023 (the "Company RRA")) pursuant to the Company RRA. For the avoidance of doubt, the Company shall comply with the provisions of Article III (Company Procedures) and Article V (Indemnification and Contribution) of the Company RRA in connection with the registration of the resale of any Warrant Stock issuable upon exercise of this Warrant.

10. Rights and Obligations Survive Exercise of Warrant. The rights and obligations of Company, of Holder of this Warrant and of the holder of shares of Warrant Stock issued upon exercise of this Warrant, contained in Sections 2, 6, 8, 9 and 18 shall survive the exercise of this Warrant.

11. Modification and Waiver. This Warrant and any provision hereof may be changed, waived, discharged or terminated only by an instrument in writing signed by the party against which enforcement of the same is sought.

12. Notices. Any notice, request or other document required or permitted to be given or delivered to Holder or Company shall be deemed to have been given (i) upon receipt if delivered personally, (ii) upon confirmation of receipt if by electronic mail or telecopy (or, if no confirmation is received, then on the next business day), (iii) one business day after the business day of deposit with a nationally recognized overnight courier, specifying next-day delivery, with written verification of receipt, or (iv) three business days after deposit in the US mail, with postage prepaid and certified or registered, to each such Holder at its address as shown on the books of Company or to Company at the address indicated therefor in the opening paragraphs of this Warrant (or at such other location as Company advises Holder in writing).

13. Survival of Certain Obligations. All of the obligations of Company relating to the Warrant Stock issuable upon the exercise of this Warrant shall survive the exercise and termination of this Warrant. All of the covenants and agreements of Company shall inure to the benefit of and be binding upon the successors and permitted assigns of Holder.

14. Descriptive Headings and Governing Law. The descriptive headings of the several sections and paragraphs of this Warrant are inserted for convenience only and do not constitute a part of this Warrant. This Warrant shall be construed and enforced in accordance with, and the rights of the parties shall be governed by, the laws of the State of New York, without giving effect to conflicts of law principles.

15. Lost Warrants or Stock Certificates. Company agrees that upon receipt of evidence reasonably satisfactory to Company of the loss, theft, destruction, or mutilation of any Warrant or stock certificate and, in the case of any such loss, theft or destruction, upon receipt of an indemnity reasonably satisfactory to Company, or in the case of any such mutilation upon surrender and cancellation of such Warrant or stock certificate, Company at its expense will make and deliver a new Warrant or stock certificate, of like tenor, in lieu of the lost, stolen, destroyed or mutilated Warrant or stock certificate.

16. Fractional Shares. No fractional shares shall be issued upon exercise of this Warrant. Company shall, in lieu of issuing any fractional share, pay the holder entitled to such fraction a sum in cash equal to such fraction multiplied by the then effective Stock Purchase Price.

17. Representations of Holder. With respect to this Warrant, Holder represents and warrants to Company as follows:

17.1 Experience. It is experienced in evaluating and investing in companies engaged in businesses similar to that of Company; it understands that investment in this Warrant involves substantial risks; it has made detailed inquiries concerning Company, its business and services, its officers and its personnel; the officers of Company have made available to Holder any and all written information it has requested; the officers of Company have answered to Holder's satisfaction all inquiries made by it; and it has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risks of investment in Company and it is able to bear the economic risk of that investment.

17.2 Investment. It is acquiring this Warrant for investment for its own account and not with a view to, or for resale in connection with, any distribution thereof. It understands that this Warrant, the shares of Warrant Stock issuable upon exercise thereof have not been registered under the Securities Act, nor qualified under applicable state securities laws. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the shares of Warrant Stock.

17.3 Rule 144. It acknowledges that this Warrant and the Warrant Stock must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. It has been advised or is aware of the provisions of Rule 144 promulgated under the Securities Act.

17.4 Access to Data. It has had an opportunity to discuss Company's business, management and financial affairs with Company's management and has had the opportunity to inspect Company's facilities. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities, including access to the Company's filings made pursuant to Section 13 of the Securities Exchange Act of 1934, as amended, on the United States Securities and Exchange Commission's Electronic Data Gathering, Analysis, and Retrieval System ("EDGAR"). Holder further has had the opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

17.5 Accredited Investor. It is an "accredited investor" within the meaning of Regulation D promulgated under the Securities Act.

18. Additional Representations and Covenants of Company. Company hereby represents, warrants and agrees as follows:

18.1 Corporate Power. Company has all requisite corporate power and corporate authority to issue this Warrant and to carry out and perform its obligations hereunder.

18.2 Authorization. All corporate action on the part of Company, its directors and stockholders necessary for the authorization, execution, delivery and performance by Company of this Warrant has been taken. This Warrant is a valid and binding obligation of Company, enforceable in accordance with its terms except as enforceability may be limited by bankruptcy, insolvency, fraudulent conveyance, reorganization or moratorium laws, other similar laws affecting creditors' rights and general principles of equity affecting the availability of specific performance and other equitable remedies.

18.3 Offering. Subject in part to the truth and accuracy of Holder's representations set forth in Section 17 hereof, the offer, issuance and sale of this Warrant is, and the issuance of Warrant Stock upon exercise of this Warrant will be exempt from the registration requirements of the Securities Act, and are exempt from the qualification requirements of any applicable state securities laws; and neither Company nor anyone acting on its behalf will take any action hereafter that would cause the loss of such exemptions.

18.4 Listing; Stock Issuance. Company shall secure and maintain the listing of the Warrant Stock issuable upon exercise of this Warrant upon each securities exchange or over-the-counter market upon which securities of the same class or series issued by Company are listed, if any. Upon exercise of this Warrant, Company will use commercially reasonable efforts to cause stock certificates representing the shares of Warrant Stock purchased pursuant to the exercise to be issued in the names of Holder, its nominees or assignees, as appropriate at the time of such exercise.

18.5 Charter Documents. Company has filed on EDGAR true and complete copies of Company's Charter, bylaws, each as amended and in effect on the date of issuance of this Warrant.

19. Counterparts; Facsimile; Electronic Mail. Each party's execution and delivery of such party's counterpart signature page to this Warrant via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, e.g., www.docusign.com) shall constitute such party's effective execution and delivery of this Warrant and agreement to and acceptance of the terms hereof for all purposes.

20. Acquisition; Replacement Warrant. In the event of either (i) an Acquisition (as defined below) of the Company, (ii) the consummation of a business combination transaction involving the Company and/or any direct or indirect parent company thereof and a publicly traded U.S. domestic special purpose acquisition company or other similar U.S. domestic corporation that is a "blank check" company under applicable U.S. securities laws and formed for the purpose of effecting such a transaction, or (iii) the consummation of a business combination transaction involving the Company and/or any direct or indirect parent company thereof with any public company listed on a U.S. securities exchange, then in the event this Warrant has not been previously exercised the Company shall cause to be issued to the Holder a replacement warrant exercisable for an equivalent number of shares of common stock of the resulting entity equal to the unexercised portion of this Warrant (the "Replacement Warrant"). The Replacement Warrant shall otherwise contain terms and conditions substantially equivalent to this Warrant. For the purpose of this Warrant, "Acquisition" means any transaction or series of related transactions involving: (A) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company; (B) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (C) any sale or other transfer by the stockholders of the Company of shares representing

at least a majority of the Company’s then-total outstanding combined voting power.

21 Notice of Certain Events. If the Company proposes at any time to:

21.1 declare any dividend or distribution upon the outstanding shares of Warrant Stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

21.2 offer for subscription or sale *pro rata* to all holders of the outstanding shares of shares of Warrant Stock any additional shares of any class or series of the Company’s stock (other than pursuant to contractual pre-emptive rights);

21.3 effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of Warrant Stock; or

21.4 effect an Acquisition or to liquidate, dissolve or wind up.

then, in connection with each such event, the Company shall give Holder:

21.5 in the case of the matters referred to in (21.1) and (21.2) above, at least ten (10) business days prior written notice of the earlier to occur of the effective date thereof or the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding Common Stock will be entitled thereto) or for determining rights to vote, if any; and

21.6 in the case of the matters referred to in (21.3) and (21.4) above at least ten (10) business days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of Common Stock will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event and such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such event giving rise to the notice).

provided, that the Company’s failure to give any such notice of such actions pursuant to this Section 21 shall not affect the validity of any such actions by the Company.

[*Remainder of this page intentionally left blank; signature page follows*]

IN WITNESS WHEREOF, Company has caused this Warrant to be duly executed by its officer, thereunto duly authorized as of the date of issuance set forth on the first page hereof.

By: /s/ Andrew Taylor
Name: Andrew Taylor
Title: Chief Financial Officer

AGREED AND ACCEPTED:

HOLDER:

AVENUE VENTURE OPPORTUNITIES FUND II, L.P.

By: Avenue Venture Opportunities Partners II, LLC
Its: General Partner
By: GL Venture Opportunities Partners II LLC
Its: Managing Member

By: /s/ Sonia Gardner
Name: Sonia Gardner
Title: Member

FORM OF SUBSCRIPTION

(To be signed only upon exercise of Warrant)

To:______________________

☐ The undersigned, the holder of the within Warrant, hereby irrevocably elects to exercise the purchase right represented by such Warrant for, and to purchase thereunder, (1) ___________ (____) shares[1] (the "Shares") of Stock of ______ and herewith makes payment of ________ Dollars ($_________) therefor, and requests that the certificates for such shares be issued in the name of, and delivered to, ____, whose address is _______.

☐ The undersigned hereby elects to convert ______ percent (%) of the value of the Warrant pursuant to the provisions of Section 1.2 of the Warrant.

The undersigned acknowledges that it has reviewed the representations and warranties contained in Section 17 of this Warrant and by its signature below hereby makes such representations and warranties to Company.

Dated ______________________

Holder: ______________________

By: ______________________

Its: ______________________

(Address)

____

____

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[1] Insert here the number of shares called for on the face of the Warrant (or, in the case of a partial exercise, the portion thereof as to which the Warrant is being exercised), in either case without making any adjustment for additional Warrant Stock or any other stock or other securities or property or cash which, pursuant to the adjustment provisions of the Warrant, may be issuable upon exercise.

ASSIGNMENT

FOR VALUE RECEIVED, the undersigned, the holder of the within Warrant, hereby sells, assigns and transfers all of the rights of the undersigned under the within Warrant, with respect to the number of shares of Warrant Stock covered thereby set forth herein below, unto:

Name of Assignee	Address	No. of Shares

Dated ____________________

Holder: ____________________

By: ____________________

Its: ____________________

EXHIBIT "A"

[On letterhead of Company]

Reference is hereby made to that certain Warrant dated October 6, 2023 issued by ORCHESTRA BIOMED HOLDINGS, INC., a Delaware corporation (the "Company"), to AVENUE VENTURE OPPORTUNITIES FUND II, L.P., a Delaware limited partnership (the "Holder").

[IF APPLICABLE] The Warrant provides that the actual number and type of shares of Company's capital stock issuable upon exercise of the Warrant and the initial exercise price per share are to be determined by reference to one or more events or conditions subsequent to the issuance of the Warrant. Such events or conditions have now occurred or lapsed, and Company wishes to confirm the actual number of shares issuable and the initial exercise price. The provisions of this Supplement to Warrant are incorporated into the Warrant by this reference, and shall control the interpretation and exercise of the Warrant.

This certifies that Holder is entitled to purchase from Company ______________, at the Holder's option, either (i) (_________) fully paid and nonassessable shares of Company's ________ Stock at a price of _______ Dollars ($_________________) per share or (ii) (_______) fully paid and nonassessable shares of Company's ______ Stock at a price of _____________ Dollars ($_______) per share.

Executed this ___ day of ________, 20___.

ORCHESTRA BIOMED HOLDINGS, INC.

By: ________________________________

Name: ________________________________

Title: ________________________________

PAUL
HASTINGS

October 10, 2023

Orchestra BioMed Holdings, Inc.
150 Union Square Drive
New Hope, Pennsylvania 18938

Re: Orchestra BioMed Holdings, Inc. Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to Orchestra BioMed Holdings, Inc., a Delaware corporation (the "***Company***"), in connection with the preparation and filing with the U.S. Securities and Exchange Commission (the "***Commission***"), pursuant to the Securities Act of 1933, as amended (the "***Securities Act***"), of the Registration Statement on Form S-1 of the Company (the "***Registration Statement***"), including a related prospectus filed with the Registration Statement (the "***Prospectus***"), relating to (a) the issuance of up to 1,932,841 shares of the Company's common stock, par value $0.0001 per share ("***Common Stock***"), upon the exercise of warrants issued by the Company, and (b) the resale of up to 22,221,440 shares of Common Stock and up to 750,000 warrants to purchase Common Stock issued by the Company and held by certain securityholders of the Company, as follows:

(i) the issuance of up to 750,000 shares of Common Stock (the "***HSAC2 Warrant Shares***") upon the exercise of 750,000 warrants issued in a private placement to the sponsor (the "***Sponsor***") of Health Sciences Acquisitions Corporation 2 ("***HSAC2***"), in connection with the initial public offering of HSAC2 (the "***HSAC2 Warrants***");

(ii) the issuance of up to 675,000 shares of Common Stock (the "***Officer and Director Warrant Shares***") upon the exercise of 675,000 warrants that were issued to certain officers and directors of the Company (the "***Officer and Director Warrants***") in connection with the forfeiture of warrants by the Sponsor as part of the business combination between Legacy Orchestra (as defined below) and HSAC2 (the "***Business Combination***");

(iii) the issuance of up to 507,841 shares of Common Stock (the "***Orchestra Warrant Shares***" and, collectively with the HSAC2 Warrant Shares and the Officer and Director Warrant Shares, the "***Warrant Shares***") upon the exercise of 507,841 warrants issued in connection with the Business Combination in exchange for warrants issued by Orchestra BioMed, Inc. ("***Legacy Orchestra***"), the Company's predecessor and now a wholly owned subsidiary of the Company (the "***Orchestra Warrants***" and, collectively with the HSAC2 Warrants and the Officer and Director Warrants, the "***Warrants***");

(iv) the resale of up to 750,000 HSAC2 Warrants (the "***Resale Warrants***") held by the Sponsor; and

(v) the resale of up to 22,221,440 shares of Common Stock (collectively, the "***Resale Shares***"), consisting of:

a. up to 10,675,809 shares of Common Stock issued to certain stockholders of the Company on January 26, 2023 in connection with the Business Combination;

b. up to 10,070,645 shares of Common Stock held by the Sponsor and its affiliates;

c. up to 22,279 shares of Common Stock issued to certain stockholders of the Company

in May 2023 in connection with the exercise of Company warrants;

d. up to 750,000 HSAC2 Warrant Shares;

e. up to 675,000 Officer and Director Warrant Shares; and

f. up to 27,707 shares of Common Stock (the "***Lender Warrant Shares***") issuable upon the exercise of warrants issued to certain lenders of the Company on October 6, 2023 (the "***Lender Warrants***").

This opinion letter is being furnished in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act.

As such counsel and for purposes of our opinions set forth herein, we have examined and relied upon originals or copies, certified or otherwise identified to our satisfaction, of such documents, resolutions, certificates and other instruments of the Company and corporate records furnished to us by the Company, and have reviewed certificates of public officials, statutes, records and such other instruments and documents as we have deemed necessary or appropriate as a basis for the opinions set forth below, including without limitation:

(i) the Registration Statement;

(ii) the Prospectus;

(iii) the Company's Certificate of Incorporation, certified as of September 20, 2023 (the "***Certificate of Incorporation***"), by the Secretary of State of the State of Delaware and certified by an officer of the Company as of the date hereof, and the Bylaws of the Company as presently in effect, certified by an officer of the Company as of the date hereof;

(iv) the Agreement and Plan of Merger, dated as of July 4, 2022, by and among the Company, HSAC2 and HSAC Olympus Merger Sub, Inc. (as amended, the "***Merger Agreement***") entered into by the parties in connection with the Business Combination;

(v) a certificate of the Secretary of State of the State of Delaware, certifying as to the existence and good standing of the Company under the laws of the State of Delaware as of September 20, 2023 (the "***Good Standing Certificate***"); and

(vi) resolutions adopted by the board of directors and/or shareholders of HSAC2, Legacy Orchestra and the Company, certified by an officer of the Company;

In such examination and in rendering the opinions expressed below, we have assumed, without independent investigation or verification: (i) the genuineness of all signatures on all agreements, instruments, corporate records, certificates and other documents submitted to us; (ii) the legal capacity, competency and authority of all persons executing all agreements, instruments, corporate records, certificates and other documents submitted to us; (iii) the authenticity and completeness of all agreements, instruments, corporate records, certificates and other documents submitted to us as originals; (iv) that all agreements, instruments, corporate records, certificates and other documents submitted to us as certified, electronic, facsimile, conformed, photostatic or other copies conform to the originals thereof, and that such originals are authentic and complete; (v) the due authorization, execution and delivery of all agreements,

instruments, corporate records, certificates and other documents by all parties thereto (other than the Company); (vi) that no documents submitted to us have been amended or terminated orally or in writing, except as has been disclosed to us in writing; (vii) that the Merger Agreement and the agreements pursuant to which the Warrants and the Lender Warrants were issued are the valid and binding obligations of each of the parties thereto (other than the Company with respect to the Resale Warrants), enforceable against such parties (other than the Company with respect to the Resale Warrants) in accordance with their respective terms; (viii) that the statements contained in the certificates and comparable documents of public officials, officers and representatives of the Company and other persons on which we have relied for the purposes of this opinion letter are true and correct on and as of the date hereof; (ix) that at or prior to the time of the issuance and delivery of any of the Warrant Shares, the Registration Statement will have been declared effective under the Securities Act; (x) that there has not been nor will there be any change in the good standing status of the Company from that reported in the Good Standing Certificate; (xi) that each of the officers and directors of the Company has properly exercised his or her fiduciary duties; (xii) that the Warrant Shares will not be issued or transferred in violation of any restriction contained in the Certificate of Incorporation. As to all questions of fact material to this opinion letter and as to the materiality of any fact or other matter referred to herein, we have relied (without independent investigation or verification) upon representations and certificates or comparable documents of officers and representatives of the Company.

With respect to the Warrants, the Warrant Shares, the Lender Warrants and the Lender Warrant Shares, we express no opinion to the extent that, notwithstanding the Company's current reservation of shares of Common Stock, future issuances of securities of the Company, including the Warrant Shares and the Lender Warrant Shares and/or antidilution adjustments to outstanding securities of the Company, including the Warrants and the Lender Warrants, may cause the Warrants and/or the Lender Warrants to be exercisable for more shares of Common Stock than the number that then remain authorized but unissued. Further, we have assumed that the exercise price of the Warrants and the Lender Warrants will not be adjusted to an amount below the par value per share of the shares of Common Stock.

Based upon the foregoing, and in reliance thereon, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that:

1. The Warrant Shares have been duly authorized by all necessary corporate action on the part of the Company and, when and if issued upon exercise of the Warrants in accordance with the terms of the respective Warrants, will be validly issued, fully paid and nonassessable.

2. The Resale Warrants constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms except as such enforceability may be limited by (i) any applicable bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally including, without limitation, fraudulent transfer or fraudulent conveyance laws; (ii) public policy considerations, statutes or court decisions that may limit rights to obtain exculpation, indemnification or contribution (including, without limitation, indemnification regarding violations of the securities laws and indemnification for losses resulting from a judgment for the payment of any amount other than in United States dollars); and (iii) general principles of equity (including, without limitation, concepts of materiality, reasonableness, good faith and fair dealing) and the availability of equitable remedies (including, without limitation, specific performance and equitable relief), regardless of whether considered in a proceeding in equity or at law.

3. The Resale Shares (other than the Warrant Shares and the Lender Warrant Shares) have been duly authorized by all necessary corporate action on the part of the Company and are validly issued, fully paid and nonassessable.

4. The Lender Warrant Shares have been duly authorized by all necessary corporate action on the part of the Company and, when and if issued upon exercise of the Lender Warrants in accordance with the terms of the Lender Warrants, will be validly issued, fully paid and nonassessable.

With regard to opinion paragraph 2: (i) our opinion is subject to the qualification that the availability of specific performance, an injunction or other equitable remedies is subject to the discretion of the court before which the request is brought; (ii) we express no opinion as to any provision of the Resale Warrants, that (a) provides for liquidated damages, buy-in damages, monetary penalties, prepayment or make-whole payments or other economic remedies to the extent such provisions may constitute unlawful penalties, (b) relates to advance waivers of claims, defenses, rights granted by law, or notice, opportunity for hearing, evidentiary requirements, statutes of limitations, trial by jury, or procedural rights, (c) restricts non-written modifications and waivers, (d) provides for the payment of legal and other professional fees where such payment is contrary to law or public policy, (e) relates to exclusivity, election or accumulation of rights or remedies, (f) authorizes or validates conclusive or discretionary determinations, or (g) provides that provisions of the Resale Warrants are severable to the extent an essential part of the agreed exchange is determined to be invalid and unenforceable; and (iii) we express no opinion as to whether a state court outside of the State of New York or a federal court of the United States would give effect to the choice of New York law provided for in the Resale Warrants.

Without limiting any of the other limitations, exceptions, assumptions and qualifications stated elsewhere herein, we express no opinion with regard to the applicability or effect of the laws of any jurisdiction other than the laws of the State of New York and the General Corporation Law of the State of Delaware as in effect on the date hereof. We are not rendering any opinion as to compliance with any federal or state antifraud law, rule or regulation relating to securities, or to the sale or issuance thereof.

This opinion letter deals only with the specified legal issues expressly addressed herein, and you should not infer any opinion that is not explicitly stated herein from any matter addressed in this opinion letter. This opinion letter is rendered solely in connection with the Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Securities Act solely for such purpose. This opinion letter is rendered as of the date hereof, and we assume no obligation to advise you or any other person with regard to any change after the date hereof in the circumstances or the law that may bear on the matters set forth herein even if the change may affect the legal analysis or a legal conclusion or other matters in this opinion letter.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the Registration Statement and to the reference to our firm in the Prospectus under the heading “Legal Matters.” In giving such consent, we do not hereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules or regulations of the Commission thereunder.

Very truly yours,

/s/ Paul Hastings LLP

Exhibit 10.30

June 10, 2021

George Papandreou, Ph.D.
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]

Re: Offer of Employment

Dear Dr. Papandreou,

We are pleased to offer you the position of Sr. Vice President, Quality at Orchestra BioMed, Inc. ("OBIO" or the "Company") and we are excited about the prospect of having you join our team. You will be reporting to Darren Sherman, President and Chief Operating Officer at OBIO. The starting date for your employment will be mutually agreed by you and the Company provided that it is no later July 12, 2021.

The following are the terms and conditions of our Offer of Employment:

1. You will be paid your base salary in 24 installments of the gross amount of $11,666.66 which is equivalent to $280,000 on an annual basis, and subject to deductions for applicable taxes and withholdings, in accordance with Company's regular payroll practices.

2. Your position with OBIO is an "exempt" position for purposes of the Federal Fair Labor Standards Act.

3. You will be working out of OBIO's New Hope, Pennsylavania office. You may be required to travel for work as necessary including to the Fort Lauderdale, Florida office.

4. You will be eligible for an annual incentive based bonus with a target of 35% of your base salary. The bonus will be awarded based on the achievement of milestones determined by the Company's Board of Directors and, if awarded, will be paid in accordance with, and subject to the terms of, OBIO's annual bonus payment practices as may be in effect from time to time.

5. In addition to your base salary and bonus compensation, you will be eligible to participate in OBIO's health benefit plans with a monthly contribution by you of 25% of the premium cost. You will also be eligible to participate in a company sponsored (non-matching) 401k plan, subject to the eligibility, vesting and other terms of these plans. Please be aware that OBIO may change its benefits plans (and any required employee contribution) as determine from time to time.

6. You will be eligible to receive equity compensation of 40,000 shares of OBIO common stock through participation in OBIO's Incentive Stock option plan that will vest as set forth in the plan. These stock options options will be granted at the fair market value of common stock at time of grant, which is $2.21 as of date of offer letter and will vest in equal quarterly installments over a period of 3 years. All grants of equity compensation are subject to approval by OBIO's Board of Directors.

7. You will also receive four weeks (20 business days) of paid vacation annually, which will be accrued based on your start date. In case of an illness, the Company also offers empoyees five paid sick days annually.

8. As OBIO's proprietary information is extremely important, this Offer of Employment is expressly subject to your signing the attached Confidentiality, Non-Competition, Non-Solicitation and and Intellectual Property Assignment Agreement.

9. In accordance with the Federal Immigration Reform and Control Act, this offer is contingent upon your satisfactorily providing documents proving your identity and demonstrating that you are authorized to work in the United States. You must complete an "I-9 form" no later than three days after your employment commences.

10. OBIO makes this offer contingent upon completion of a satisfactory background investigation, including, but not limited to, verification of former employment, professional certifications, criminal record, designations or licenses, and general financial information (including, without limitation, academic, business, and other references). If we elect to conduct a background investigation, you will be asked to sign a separate background investigation authorization form.

11. If you are not legally able to work in the United States, if you fail to consent to a background investigation or any part of the background investigation proves unsatisfactory to OBIO, we reserve the right to rescind this offer of employment or terminate your employment immediately without any prior notice to you.

12. This Offer of Employment supersedes any prior verbal or written representations and does not constitute a guarantee of employment. Your employment with OBIO will be "at-will." This means that both you and OBIO have the right to terminate your employment at any time, with or without cause, and without further obligation to you other than payment of amounts that are required under applicable law.

13. Payments to you hereunder are subject to applicable federal, state and local wage withholding requirements.

14. This Offer of Employment shall be interpreted in accordance with the laws of the State of Florida, without regard to the conflicts of laws principles that might direct application of the laws of any other jurisdiction. By accepting employment, you consent to the exclusive jurisdiction of the appropriate state or federal court located in Broward County, Florida as the venue for any claims arising out of or relating to this Offer of Employment or your employment with OBIO (or any of its subsidiaries, affiliates, parents, successors or assigns). You acknowledge that you are subject to the jurisdiction of such courts and waive any objection to such courts as being inconvenient forums. Both you and OBIO knowingly and voluntarily waive any right to trial by jury in any action arising out of or relating to this offer letter or your employment with OBIO or any of its subsidiaries, affiliates, parents, successors or assigns.

15. Lastly, the Company understands you have continuing contractual obligations to your former employer, and we intend for you to comply with those obligations. Accordingly, you agree that you will, in all respects while employed by the Company, comply with your contractual obligations to your former employer. Without limiting the foregoing, in accepting employment with OBIO and signing below, you represent that (i) you have not taken or downloaded to your computer, to any USB or to any other electronic device, and/or will return without retaining copies, all trade secret, proprietary, or other confidential information and any other materials which belong to any of your former employer(s); (ii) in connection with your OBIO employment, you will not use or disclose any trade secret, proprietary or other confidential information which belongs to your former employer(s) and if any OBIO employee asks you to use or disclose any trade secret, proprietary or other confidential information belonging to a former employer you shall promptly notify Darren Sherman; (iii) you are not party to any agreement or subject to any policy that would prevent or restrict you from engaging in activities competitive with the activities of your former employer(s) or, if you are subject to such an agreement or policy, you have complied and will comply with it; (iv) you have not solicited or encouraged, and will not request, solicit or encourage, any employees or customers/clients of your former employer(s) to join OBIO in violation of any contractul or common-law obligation or duty to your past employer(s); and (v) you are not subject to any agreement or policy that requires you to provide

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notice of your resignation to your prior employer(s) in order for such resignation to become effective (or if you are subject to such agreement or policy, you have provided notice, and the notice will have elapsed before your scheduled start date with OBIO).

* * * *

We look forward to a successful and mutually rewarding working relationship. If you have any questions regarding the above, please feel free to call Darren Sherman. This offer is contingent upon your written acceptance prior to 5:00 pm EDT on June 21, 2021.

My signature below indicates that I accept this offer of employment, conditioned upon the terms discussed above. I understand the terms of this offer letter supersede any prior representations or terms made by the Company or any representative of the Company, whether expressed orally or in writing.

Orchestra BioMed, Inc.	**Accepted and Agreed:**
By: /s/ Darren R. Sherman	/s/ George Papandreou
Darren R. Sherman	George Papandreou
President and COO	June 21, 2021

January 16, 2023

George Papandreou
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]

Promotion

Dear George:

Congratulations on your promotion to Senior Vice President & General Manager Focal Therapies. Your new position, located in our New Hope office is effective January 16, 2023. In this role you will continue to report to Darren Sherman, President, and COO. Your new annual salary will be $325,000 or $13,541.67 semi-monthly. Your compensation continues to be subject to deductions for applicable taxes and withholdings, in accordance with Company's regular payroll practices. All your other benefits will remain the same.

Again, Congratulations on the new position. We look forward to your continued success at Orchestra BioMed. If you have any questions regarding the terms of this promotion, please contact Lisa Daniels, Senior HR Director.

Sincerely,

/s/ Darren Sherman
President and COO
Orchestra BioMed

Acknowledged and Accepted:

/s/ George Papandreou	1/16/2023
Employee, George Papandreou	Date

Exhibit 10.32

May 24, 2023

William Little
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]
[Omitted pursuant to Item 601(a)(6)]

Re: Offer of Employment

Dear Bill,

We are pleased to offer you the position of Executive Vice President, Corporate Development & Strategy of Orchestra BioMed, Inc. ("Orchestra BioMed" or the "Company") and are excited about the prospect of having you join our team. You will be reporting to David Hochman, Chairman, CEO & Founder (the "CEO") with an estimated start date of June 1, 2023.

The following are the terms and conditions of our Offer of Employment:

1. Your will serve as Executive Vice President, Corporate Development & Strategy of the Company. Your position will be remote with the expectation is that you will travel as needed based on business needs and will be expected to spend approximately 1 week per month at the Company's office in New York City or at one of the Company's other offices as agreed by you and the CEO.

2. You will be paid a base salary in 24 semi-monthly installments of $15,208.33 each**,** which is equivalent to a gross salary of $365,000 on an annual basis, subject to deductions for applicable taxes and withholdings, in accordance with the Company's regular payroll practices.

3. Your position with Orchestra BioMed is an "exempt" position for purposes of the Federal Fair Labor Standards Act. In addition, your position is "at will" meaning your employment may be terminated by either you or Orchestra BioMed at any time and for any reason; provided, however, the Company requests you provide customary notice in the event of your voluntary resignation and, in the event of certain terminations, you will be eligible for additional payments as provided herein (relating to severance).

4. You will be eligible for a two part annual incentive-based bonus. The primary bonus will have a target of 35% of your base salary which will be awarded based on the achievement of milestones determined by the Company's Board of Directors or its Compensation Committee as well as the achievement of individual objectives determined by you and your manager. If awarded, the Annual Bonus would be paid in accordance with, and subject to the terms of, Orchestra BioMed's annual bonus payment practices as may be in effect from time to time. In addition you will be recommended to receive a Strategic Partnership Bonus with potential earn out up to 35% of your annual base salary based on the completion of corporate partnerships including up front investments and/or payments, with any such bonus to be subject to approval by the Company's Board of Directors or its Compensation Committee in connection with any such completion. In order to be eligible for any bonus, you must be employed and in good standing on the date of payment.

5. You will be eligible to receive an initial equity grant of 250,526 restricted stock units (RSUs) of Orchestra BioMed Holdings, Inc. ("Parent") through participation in Orchestra BioMed Holdings

Inc.’s 2023 Equity Incentive Plan (the “Plan”). Alternatively, you may instead choose to be eligible to receive an award of non-qualified stock options under the Plan covering 375,789 shares of Parent common stock, with an exercise price equal to fair market value on the date of grant. In either case, the award will be granted on the same date as the 2023 Orchestra BioMed Holdings Inc.’s annual stock incentive grant to employees, including the CEO and President & COO, and will reflect Parent’s standard and terms and conditions for equity compensation awards. If options, the award will vest over four years, with one-fourth vesting on the first anniversary of your start date and with the remainder vesting in quarterly installments over the next three years on your employment anniversary, subject, in all cases, to your continued employment. If RSUs, the award will vest in substantially equal installments at the end of each anniversary of your start date over a period of at least three years to be determined by Parent’s Board of directors (with the actual vesting schedule, which may be longer than three years, to be consistent with Parent’s standard vesting schedule for RSU awards). You will be eligible to receive additional equity grants based on Company policy and performance. All grants of equity compensation are subject to approval by Parent’s Board of Directors.

6. In addition to your base salary and bonus compensation, you will be eligible to participate in Orchestra BioMed’s health benefit plans (currently with a monthly contribution by you of 10% of the premium cost) and a Company-sponsored (matching) 401k plan, subject to the eligibility and other terms of these plans. Please be aware that the Company may change its benefit plans (and any required employee contribution) as it may determine from time to time at its sole discretion.

7. You will receive 4 weeks (20 business days) of paid vacation annually, which will be accrued based on your start date. In case of illness, the Company also offers employees five (5) paid sick days annually.

8. If your employment is terminated without Cause or for Good Reason (as defined by Exhibit A) and conditioned on your execution in favor of the Company (including its subsidiaries and affiliates and its and their officers, directors, and employees) of a general release of all claims, in a form acceptable to the Company in its sole discretion, such that the general release becomes irrevocably effective within 60 days following the termination of your employment, the Company will pay or provide you with severance consisting of (i) continued base salary (subject to deductions and withholdings) for the Severance Period of nine (9) months; (ii) COBRA reimbursement during the nine (9) month Severance Period (or, if earlier, until you become eligible for benefits from a subsequent employer) based on your elections at termination if you validly elect to continue your medical benefits under applicable law, and (iii) accelerated vesting of the equity award referred to in paragraph 5 above so that such award is vested to the same extent it would be vested had your employment continued for the duration of the Severance Period. The continued salary component of severance will accrue from the date of termination, with accrued amounts paid on the first regularly scheduled payroll that occurs more than 60 days following the termination of employment (but subject to paragraph 15 below). Reimbursement of COBRA premiums will be provided in accordance with the Company’s standard expense reimbursement procedures and practices subject to you submitting proof of payment within 30 days of paying the applicable premium.

9. As Orchestra BioMed’s proprietary information is extremely important, this Offer of Employment is expressly subject to your signing the attached Confidentiality, Non-Competition, Non-Solicitation and and Intellectual Property Assignment Agreements.

10. In accordance with the Federal Immigration Reform and Control Act, this offer is contingent upon your satisfactorily providing documents proving your identity and demonstrating that you are

authorized to work in the United States. You must complete an "I-9 form" no later than three days after your employment commences.

11. Orchestra BioMed makes this offer contingent upon completion reference checks and a satisfactory background investigation, including, but not limited to, verification of education, former employment, professional certifications, criminal record, designations or licenses, and general financial information (including, without limitation, academic, business, and other references). If we elect to conduct a background investigation, you will be asked to sign a separate background investigation authorization form.

12. If you are not legally able to work in the United States, if you fail to consent to a background investigation or any part of the background investigation proves unsatisfactory to Orchestra BioMed, we reserve the right to rescind this Offer of Employment or terminate your employment immediately without any prior notice to you.

13. This letter supersedes any prior verbal or written representations and does not constitute a guarantee of employment. Your employment with Orchestra BioMed will be "at-will." This means that both you and Orchestra BioMed have the right to terminate your employment at any time, with or without cause, and without further obligation to you other than payment of amounts that are required under applicable law.

14. Payments to you hereunder are subject to applicable federal, state and local wage withholding requirements.

15. This Offer of Employment is intended to meet the requirements of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), and the regulations promulgated thereunder ("Section 409A") and will be interpreted and construed consistent with that intent. For purposes of this Offer of Employment, the terms "terminate," "terminated" and "termination" with respect to payment of nonqualified deferred compensation under Section 409A means a termination of your employment that constitutes a "separation from service" within the meaning of the default rules of Section 409A of the Code. Each payment provided hereunder (including, without limitation, each payment of the continued base salary component of severance) shall be treated as a separate and distinct payment for purposes of Section 409A. Notwithstanding any other provision of this Offer of Employment, to the extent that the right to any payment hereunder provides for the "deferral of compensation" within the meaning of Section 409A(d)(1) of the Code, the payment will be paid (or provided) in accordance with the following:

    a. if you are a "Specified Employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code on the date of your termination of employment, then no such payment shall be made or commence during the period beginning on the date of termination and ending on the date that is six (6) months following the date of termination or, if earlier, on the date of your death. The amount of any payment that would otherwise be paid to you during this period will instead be paid on the fifteenth (15th) day of the first calendar month following the end of the period; and

    b. payments with respect to reimbursements of expenses shall be made in accordance with applicable company policy but in all cases on or before the last day of the calendar year following the calendar year in which the relevant expense is incurred. The amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year.

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16. The terms of this Offer of Employment shall be interpreted in accordance with the laws of the State of Florida, without regard to the conflicts of laws principles that might direct application of the laws of any other jurisdiction. By accepting employment, you consent to the exclusive jurisdiction of the appropriate state court located in Broward County, Florida or, if jurisdiction is appropriate, the United States District Court for the Southern District of Florida (Ft. Lauderdale Division) as the venue for any claims arising out of or relating to this Offer of Employment or your employment with Orchestra BioMed (or any of its subsidiaries, affiliates, parents, successors, or assigns). You acknowledge that you are subject to the jurisdiction of such courts and waive any objection to such courts as being inconvenient forums. You agree that if you (or someone acting on your behalf) initiate any action arising out of or relating to this Offer of Employment or your employment with Orchestra BioMed (or any of its subsidiaries, affiliates, parents, successors, or assigns) in any court other than the Florida courts identified in this paragraph 16, you will not object to and will assist Orchestra BioMed (or any of its subsidiaries, affiliates, parents, successors, or assigns) in its efforts to dismiss or transfer such action to the appropriate Florida court, consistent with the terms of this paragraph 16. Both you and Orchestra BioMed knowingly and voluntarily waive any right to trial by jury in any action arising out of or relating to this Offer of Employment or your employment with Orchestra BioMed or any of its subsidiaries, affiliates, parents, successors, or assigns.

17. Lastly, the Company expects you to comply with any continuing legal or contractual obligations you may have to your former employer. Accordingly, you agree that you will, in all respects while employed by the Company, comply with such obligations to your former employer. Without limiting the foregoing, in accepting employment with Orchestra BioMed and signing below, you represent that (i) you have not taken or downloaded to your computer, to any USB or to any other electronic device, and/or will return without retaining copies, all trade secret, proprietary, or other confidential information and any other materials which belong to any of your former employer(s); (ii) in connection with your Orchestra BioMed employment, you will not use or disclose any trade secret, proprietary or other confidential information which belongs to your former employer(s) and if any Orchestra BioMed employee asks you to use or disclose any trade secret, proprietary or other confidential information belonging to a former employer you shall promptly notify Darren Sherman; (iii) you are not party to any agreement or subject to any policy that would prevent or restrict you from engaging in activities competitive with the activities of your former employer(s) or, if you are subject to such an agreement or policy, you have complied and will comply with it; (iv) you have not solicited or encouraged, and will not request, solicit or encourage, any employees or customers/clients of your former employer(s) to join Orchestra BioMed in violation of any contractual or common-law obligation or duty to your past employer(s); and (v) you are not subject to any agreement or policy that requires you to provide notice of your resignation to your prior employer(s) in order for such resignation to become effective (or if you are subject to such agreement or policy, you have provided notice, and the notice will have elapsed before your scheduled start date with Orchestra BioMed).

* * * *

We look forward to a successful and mutually-rewarding working relationship. If you have any questions regarding the above, please feel free to call Lisa Daniels, Senior Director, Human Resources at [Omitted pursuant to Item 601(a)(6)]. This offer is contingent upon your written acceptance within three business days.

Orchestra BioMed, Inc.	**Accepted and Agreed:**
By: /s/ David Hochman	/s/ William R. Little
David Hochman	William Little
Chairman, CEO & Founder	
Date 5/27/2023	Date 5/25/2023

Exhibit A

For the purposes of this letter, "Cause" shall be determined soley by Orchestra BioMed Inc Board of Directors (excluding William Little ("Employee") if he is a member of the Board of Directors), and includes, but is not limited to, the following:

i. Employee's willful engagement in dishonesty, breach of trust, unethical business conduct, illegal conduct or gross misconduct;

ii. Employee's embezzlement, misappropriation or fraud, whether or not related to Employee's employment with the Company;

iii. Employee's arrest or conviction of a plea of guilty or nolo contendere to a crime that constitutes a felony (or state law equivalent) or a crime that consistitues a misdemeanor involving moral turpitude, fraud or misrepresentation (whether or not related to Employee's employment with the Company);

iv. Employee's commission of any willful or intentional act that could reasonably be expected to injure the reputation, business, or business relationships of the Company, notice of which shall have been delivered to Employee by the Board of Directors, and which identifies the manner in which the Company believes Employee has engaged in such acts;

v. Employee's violation of material policy of the Company, notice of which shall have been delivered to Employee by the Board of Directors, and which identifies the manner in which the Company believes Employee has engaged in intentional commission of any such policy violation, and Employee has failed to remedy such failure, within the fifteen (15) day period immediately following receipt of the notice of such failure (unless the policy breach is one that, in the Company's determination, cannot be remedied after-the-fact, e.g., intentional discrimination, sexual harassment, workplace violence, etc.);

vi. Employee's use, possession, or being under the influence of illegal drugs (or abuse of prescription drugs) on the Company's premises or at a Company-related event;

vii. Employee's willful unauthorized, disclosure of Confidential Information (as defined in the Company Confidentiality, Non-Competition, Non-Solicitation and Intellectual Property Assignment Agreement);

viii. Employee's failure to cooperate in an internal investigation;

ix. Employee's material breach of any obligations to the Company; and

x. Continued or excessive absences or tardiness, after an official warning has been issued to Employee and failure to cure (not including authorized) leaves of absence, FMLA leave, or absences that are a result of accommodation under the Americans with Disabilities Act);

"Good Reason" means (i) the Company fails to pay or provide when due (or, with respect to the Employee's salary, there is an unauthorized deduction in) the Employee's salary , or (ii) there is a

material reduction in the benefits provided to Employee under this letter unless such reduction is reasonably commensurate with a reduction in benefits made available to all employees of the Company; provided, however, the Employee's resignation is for Good Reason only if (1) Employee notifies the Company of the potential Good Reason trigger within 30 days of learning of the potential trigger, (2) the Company fails to cure the potential Good Reason trigger within 30 days following receipent of notice from the Employee, and (3) the Employee resigns within 30 days following the expiration of the foregoing 30-day cure period.

Exhibit 23.1

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Orchestra BioMed Holdings, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Orchestra BioMed Holdings, Inc. (the Company) as of December 31, 2021 and 2022 the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2022, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.

Philadelphia, Pennsylvania

March 24, 2023, except for the Business Combination Transaction paragraphs in Note 1, and the last three paragraphs of Note 14, as to which the date is October 10, 2023

Exhibit 107

Calculation of Filing Fee Tables

Form S-1
(Form Type)

Orchestra BioMed Holdings, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount to be Registered[1]	Proposed Maximum Offering Price Per Security	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Newly Registered Securities								
Fees to be Paid	Equity	Common Stock, par value $0.0001 per share	457(g)	1,425,000[2]	$11.50[3]	$16,387,500.00	$0.00014760	$2,418.80
	Equity	Common Stock,par value $0.0001 per share	457(g)	507,841[4]	$9.01[5]	$4,575,647.41	$0.00014760	$675.37
	Equity	Common Stock, par value $0.0001 per share	457(c)	22,221,440[6]	$6.82[7]	$151,550,220.80	$0.00014760	$22,368.81
	Equity	Warrants to purchase Common Stock	457(i)	750,000[8]	—	—	—	—[9]
Fees previously Paid	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Total Offering Amounts					$172,513,368.21		$25,462.98
	Total Fees Previously Paid							—
	Total Fee Offsets							—
	Net Fee Due							$25,462.98

(1) Pursuant to Rule 416(a) promulgated under the U.S. Securities Act of 1933, as amended (the "Securities Act"), there are also being registered an indeterminable number of additional securities as may be issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.

(2) Consists of 1,425,000 shares of common stock, par value $0.0001 per share (the "Common Stock"), of Orchestra BioMed Holdings, Inc. (the "Company"), issuable upon the exercise of (i) 750,000 HSAC2 Warrants (as defined in this registration statement) by the holders thereof and (ii) 675,000 Officer and Director Warrants (as defined in this registration statement) by the holders thereof.

(3) The price per share is the exercise price per HSAC2 Warrant and per Officer and Director Warrant of $11.50 per share.

(4) Consists of 507,841 shares of Common Stock, issuable upon the exercise of 507,841 Orchestra Warrants (as defined in this registration statement) by the holders thereof.

(5) The price per share is the weighted average exercise of the Orchestra Warrants of $9.01 per share.

(6) Consists of 22,221,440 shares of Common Stock registered for resale by the Selling Securityholders named in this registration statement, including (i) 10,675,809 Orchestra Affiliate Shares (as defined in this registration statement); (ii) 10,070,645 Sponsor Shares (as defined in this registration statement); (iii) 22,279 shares of Common Stock issued to certain Selling Stockholders in May 2023 in connection with the exercise of Company warrants, (iv) 750,000 shares of Common Stock issuable upon the exercise of HSAC2 Warrants by the holders thereof; (v) 675,000 shares of Common Stock issuable upon the exercise of Officer and Director Warrants by the holders thereof and (vi) 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company.

(7) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(c) under the Securities Act. The proposed maximum offering price per is based on the average of the high and low prices of the Common Stock on the Nasdaq Global Market on October 9, 2023 (such date being within five business days prior to the date that this registration statement was filed with the U.S. Securities and Exchange Commission).

(8) Represents the resale of 750,000 HSAC2 Warrants.

(9) In accordance with Rule 457(i), the entire registration fee for the HSAC2 Warrants is allocated to the shares of Common Stock underlying such warrants, and no separate fee is payable for the HSAC2 Warrants.