

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

PRE-EFFECTIVE AMENDMENT NO. 1  
TO  
**FORM S-1 ON FORM S-3**  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

**ORCHESTRA BIOMED HOLDINGS, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**3841**  
(Primary Standard Industrial  
Classification Code Number)

**92-2038755**  
(I.R.S. Employer  
Identification No.)

**150 Union Square Drive  
New Hope, Pennsylvania 18938  
(212) 862-5797**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**David P. Hochman  
150 Union Square Drive  
New Hope, Pennsylvania 18938  
(212) 862-5797**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies to:**

**Samuel Waxman, Esq.  
Yariv Katz, Esq.  
Keith Pisani, Esq.  
Paul Hastings LLP  
200 Park Avenue  
New York, NY 10016  
Tel: (212) 318-6000**

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

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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, other than securities offered only in connection with dividend or interest reinvestment plans, 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, please 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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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.**

**EXPLANATORY NOTE**

On October 10, 2023, Orchestra BioMed Holdings, Inc. (the “Company”) filed a registration statement with the Securities and Exchange Commission on Form S-1 (File No. 333-274924) (the “Registration Statement”). This Pre-Effective Amendment No. 1 to Form S-1 on Form S-3 is being filed by the Company to convert the Registration Statement into a registration statement on Form S-3.

The information included in this filing amends the Registration Statement and the prospectus contained therein. No additional securities are being registered under this Pre-Effective Amendment and all applicable registration and filing fees were paid at the time of the original filing of the Registration Statement.

---

**SUBJECT TO COMPLETION, DATED MARCH 27, 2024**

**PRELIMINARY PROSPECTUS**

**ORCHESTRA BIOMED HOLDINGS, INC.**

**Up to 18,586,201 Shares of Common Stock  
Up to 1,917,841 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 1,917,841 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, with an exercise price of \$11.50 per share (the “HSAC2 Warrant Shares”), issued in a private placement to HSAC 2 Holdings, LLC, 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 660,000 shares of Common Stock issuable upon the exercise of 660,000 warrants, with an exercise price of \$11.50 per share (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 (as defined below) (90,000 of the initial 750,000 Officer and Director Warrants were forfeited in connection with the departure of Orchestra’s former Chief Financial Officer and one Orchestra director); and
- (c) up to 507,841 shares of Common Stock issuable upon the exercise of 507,841 private warrants, with a weighted average exercise price of \$9.01 per share (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 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 18,586,201 shares (the “Resale Shares”) of Common Stock, consisting of the securities listed below.
  - (i) up to 7,077,849 shares of Common Stock issued to certain selling stockholders (the “Orchestra Affiliate Shares”), with a weighted average cost per share of \$7.26;
  - (ii) up to 10,070,645 shares of Common Stock held by the Sponsor and certain entities related to the Sponsor (the “Sponsor and Related Party Shares”), with a weighted average cost per share of \$5.80;
  - (iii) up to 750,000 HSAC2 Warrant Shares that could be acquired upon the exercise of the HSAC2 Warrants and payment of the exercise price of \$11.50 per share;
  - (iv) up to 660,000 Officer and Director Warrant Shares that could be acquired upon the exercise of the Officer and Director Warrants and payment of the exercise price of \$11.50 per share; and
  - (v) up to 27,707 shares of Common Stock issuable upon the exercise of warrants issued to certain lenders of the Company (the “Lender Warrants”) that could be acquired upon the exercise of the Lender Warrants and payment of the exercise price of \$7.67 per share;
- (b) the Sponsor (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 for which the Sponsor paid \$1.00 per HSAC2 Warrant in connection with the initial public offering of HSAC2 (the “HSAC2 IPO”).

For more information about the securities offered for resale by the Selling Securityholders pursuant to this prospectus, including the purchase prices paid by such Selling Securityholders for their securities, see “*Information Related to the Offered Securities*” beginning on page 6 of this prospectus.

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.

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”).

Due to the significant number of redemptions of HSAC2’s ordinary shares in connection with the Business Combination, there was a significantly lower number of HSAC2 ordinary shares that converted into shares of our Common Stock in connection with the Business Combination. As a result, the shares of our Common Stock being registered for resale (a portion of which may not be resold until the expiration of the applicable lock-up period) are anticipated to constitute a considerable percentage of our public float. Additionally, a significant portion of the shares of our Common Stock being registered for resale were originally purchased by Selling Securityholders pursuant to investments in Legacy Orchestra at prices considerably below the current market price of our Common Stock. This discrepancy in purchase prices may have an impact on the market perception of our Common Stock’s value and could increase the volatility of the market price of our Common Stock or result in a significant decline in the public trading price of our Common Stock. The registration of these shares for resale creates the possibility of a significant increase in the supply of our Common Stock in the market. The increased supply, coupled with the potential disparity in purchase prices, may lead to heightened selling pressure, which could negatively affect the public trading price of our Common Stock. We will not receive any proceeds from the resale of Common Stock by the Selling Securityholders pursuant to this prospectus.

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 16 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. We will receive up to an aggregate of approximately \$21.0 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. We believe the likelihood that warrant holders will exercise their Warrants, and therefore the amount of cash proceeds that we would receive, is dependent upon the market price of our Common Stock. As further discussed in this prospectus, as of the date of this prospectus, the HSAC2 Warrants, the Officer and Director Warrants and a significant portion of the Orchestra Warrants, are “out of the money,” meaning the exercise price is higher than the market price of our Common Stock. Holders of such “out of the money” Warrants are not likely to exercise such Warrants.

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 March 26, 2024, the last reported sales price per share of our Common Stock was \$5.26.

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 headings “*Where You Can Find More Information*” and “*Incorporation of Certain Information by Reference*,” and any amendments or supplements carefully before you invest in any of our securities.

**Investing in our common stock involves substantial risks. See “Risk Factors” Beginning on page 8 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 , 2024

## TABLE OF CONTENTS

<a href="#"><u>ABOUT THIS PROSPECTUS</u></a>	<a href="#"><u>iii</u></a>
<a href="#"><u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u></a>	<a href="#"><u>iv</u></a>
<a href="#"><u>SUMMARY OF THE PROSPECTUS</u></a>	<a href="#"><u>1</u></a>
<a href="#"><u>The Company</u></a>	<a href="#"><u>1</u></a>
<a href="#"><u>Emerging Growth Company and Smaller Reporting Company Status</u></a>	<a href="#"><u>1</u></a>
<a href="#"><u>THE OFFERING</u></a>	<a href="#"><u>3</u></a>
<a href="#"><u>USE OF PROCEEDS</u></a>	<a href="#"><u>9</u></a>
<a href="#"><u>DETERMINATION OF OFFERING PRICE</u></a>	<a href="#"><u>10</u></a>
<a href="#"><u>SELLING SECURITYHOLDERS</u></a>	<a href="#"><u>11</u></a>
<a href="#"><u>PLAN OF DISTRIBUTION</u></a>	<a href="#"><u>16</u></a>
<a href="#"><u>MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS</u></a>	<a href="#"><u>21</u></a>
<a href="#"><u>U.S. Holders</u></a>	<a href="#"><u>22</u></a>
<a href="#"><u>Non-U.S. Holders</u></a>	<a href="#"><u>24</u></a>
<a href="#"><u>DESCRIPTION OF SECURITIES</u></a>	<a href="#"><u>27</u></a>
<a href="#"><u>General</u></a>	<a href="#"><u>27</u></a>
<a href="#"><u>Authorized and Outstanding Stock</u></a>	<a href="#"><u>27</u></a>
<a href="#"><u>Common Stock</u></a>	<a href="#"><u>27</u></a>
<a href="#"><u>Preferred Stock</u></a>	<a href="#"><u>27</u></a>
<a href="#"><u>Outstanding Warrants</u></a>	<a href="#"><u>28</u></a>
<a href="#"><u>Piggyback Registration Rights</u></a>	<a href="#"><u>30</u></a>
<a href="#"><u>Registration Rights and Lock-Up Agreement</u></a>	<a href="#"><u>30</u></a>
<a href="#"><u>Anti-Takeover Effects of our Governing Documents under Delaware Law</u></a>	<a href="#"><u>31</u></a>
<a href="#"><u>Listing</u></a>	<a href="#"><u>33</u></a>
<a href="#"><u>Transfer Agent and Registrar</u></a>	<a href="#"><u>33</u></a>
<a href="#"><u>LEGAL MATTERS</u></a>	<a href="#"><u>33</u></a>
<a href="#"><u>EXPERTS</u></a>	<a href="#"><u>33</u></a>
<a href="#"><u>WHERE YOU CAN FIND MORE INFORMATION</u></a>	<a href="#"><u>33</u></a>
<a href="#"><u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u></a>	<a href="#"><u>34</u></a>

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 or incorporated by reference into 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 or incorporated by reference into 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-3 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 or incorporated by reference into 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*” and “*Incorporation of Certain Information by Reference*.”

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 or incorporated by reference into this prospectus, 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 or incorporated by reference into this prospectus include, but are not limited to, statements about:

- our ability to raise financing in the future;
- 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 prospectus and are subject to a number of risks, uncertainties, and assumptions referred to under the heading “Risk Factors” on page 8 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, except as required by law.

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 prospectus, 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 or incorporated by reference in this prospectus. Before making your investment decision with respect to our securities, you should carefully read this entire prospectus, including the information referred to under “Risk Factors” and “Incorporation of Certain Information by Reference” and the financial statements incorporated by reference into 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 lead product candidate is BackBeat Cardiac Neuromodulation Therapy (“BackBeat CNT”) for the treatment of hypertension (“HTN”), the leading risk factor for death worldwide. We have an exclusive license and collaboration agreement (the “Medtronic Agreement”) with Medtronic, Inc. (“Medtronic”) for the development and commercialization of BackBeat CNT for the treatment of HTN in patients indicated for a cardiac pacemaker. We are also developing the 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 Terumo Medical Corporation (“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.

### **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.

## THE OFFERING

<b>Issuer</b>	Orchestra BioMed Holdings, Inc.
<b>Issuance of Common Stock</b>	
Shares of Common Stock offered by us	Up to 1,917,841 shares of Common Stock, issuable upon the exercise of (i) 750,000 HSAC2 Warrants and (ii) 660,000 Officer and Director Warrants and (iii) 507,841 Orchestra Warrants.
Shares of Common Stock outstanding prior to exercise of all Warrants <sup>(1)</sup>	35,777,412 shares (as of March 22, 2024).
Shares of Common Stock outstanding assuming exercise of all Warrants <sup>(2)</sup>	37,722,960 shares (based on total shares outstanding as of March 22, 2024).
Use of Proceeds	We will receive up to an aggregate of approximately \$21.0 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. As of the date of this prospectus, the HSAC2 Warrants, the Officer and Director Warrants and a significant portion of the Orchestra Warrants, are “out-of-the money,” meaning the exercise price is higher than the market price of our Common Stock. We do not expect holders of such “out of the money” Warrants to exercise such Warrants and, therefore, we do not expect to receive cash proceeds from any such exercise, for so long as such Warrants remain “out-of-the money.” See “ <i>Use of Proceeds</i> ” elsewhere in this prospectus.
<b>Resale of Common Stock and Warrants</b>	
Shares of Common Stock offered by the Selling Securityholders	Up to 18,586,201 shares of Common Stock, consisting of: <ul style="list-style-type: none"> <li>(i) up to 7,077,849 Orchestra Affiliate Shares, with a weighted average cost per share of \$7.26;</li> <li>(ii) up to 10,070,645 Sponsor and Related Party Shares, with a weighted average cost per share of \$5.80;</li> <li>(iii) up to 750,000 HSAC2 Warrant Shares that could be acquired upon the exercise of the HSAC2 Warrants and payment of the exercise price of \$11.50 per share;</li> <li>(iv) up to 660,000 Officer and Director Warrant Shares that could be acquired upon the exercise of the Officer and Director Warrants and payment of the exercise price of \$11.50 per share; and</li> <li>(v) up to 27,707 shares of Common Stock that could be</li> </ul>

	<p>acquired upon the exercise of the Lender Warrants and payment of the exercise price of \$7.67 per share.</p> <p>For more information about the securities offered for resale by the Selling Securityholders pursuant to this prospectus, including the purchase prices paid by such Selling Securityholders for their securities, see “<i>Information Related to the Offered Securities</i>” beginning on page 6 of this prospectus.</p>
Warrants offered by the Selling Warrantholder	<p>Up to 750,000 HSAC2 Warrants, consisting of the HSAC2 Warrants not forfeited by the Sponsor as part of the Business Combination. 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.</p>
Use of Proceeds	<p>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.</p>
<b>Lock-Up Restrictions</b>	<p>Certain of our stockholders are subject to certain restrictions on transfer until the termination of applicable lock-up periods as described in our filings with the SEC incorporated by reference herein. See “<i>Incorporation of Certain Information by Reference</i>” herein.</p>
<b>Market for Common Stock</b>	<p>Our Common Stock is currently traded on the Nasdaq Global Market under the symbol “OBIO”.</p>
<b>Risk Factors</b>	<p>See “<i>Risk Factors</i>” beginning on page 8 and other information included in or incorporated by reference into this prospectus for a discussion of factors you should carefully consider before deciding to invest in the securities being offered by this prospectus.</p>
<hr/> <p>(1) The number of shares of Common Stock outstanding is based on an aggregate of 35,777,412 shares outstanding as of March 22, 2024, and excludes:</p> <ul style="list-style-type: none"> <li>(a) 3,705,918 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 \$7.77 per share;</li> <li>(b) 759,575 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 \$7.45 per share;</li> <li>(c) 1,671,055 shares of Common Stock issuable upon the vesting of restricted stock units outstanding under the 2023 Plan;</li> <li>(d) up to 2,931,880 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 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);</li> </ul>	

- (e) approximately 4,000,000 shares of Common Stock to be issued if certain earnout milestones are 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) 660,000 shares of Common Stock issuable upon the exercise of the Officer and Director Warrants, with an exercise price of \$11.50 per share;
  - (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 the Lender Warrants, with an exercise price of \$7.67 per share.
- (2) The number of shares of Common Stock outstanding is based on an aggregate of 35,777,412 shares outstanding as of March 22, 2024, and excludes (a) through (e) in footnote (1) above.

### INFORMATION RELATED TO THE OFFERED SECURITIES

As shown in the table below, the Sponsor and some of the other Selling Securityholders may realize a positive rate of return on the sale of their shares of Common Stock covered by this prospectus. While some of the Selling Securityholders may experience a positive rate of return based on the current trading price, most of the Selling Securityholders and the public securityholders may not experience a similar rate of return on the securities they purchased due to differences in the purchase prices they paid and the trading price of our Common Stock when they elect to sell. Such securityholders may instead experience a negative rate of return on their investment. The weighted average purchase price of the shares of our common stock being registered for resale pursuant to the Second Amended and Restated Registration Rights and Lock-Up Agreement (excluding shares underlying outstanding Warrants) was \$6.65 per share. On March 26, 2024, the last reported sales price per share of our Common Stock on the Nasdaq Global Market was \$5.26.

The following table includes information relating to the shares of Common Stock registered for resale hereby, including the purchase price each category of Selling Securityholder paid for its securities and the potential profit relating to such securities. The following table is in part based off our internal records and is for illustrative purposes only. The table should not be relied upon for any purpose outside of its illustrative nature.

Selling Securityholder and Securities	Number of Resale Shares/Warrants	Purchase Price per Resale Share/Warrant <sup>(1)</sup>	Aggregate Purchase Price <sup>(1)</sup>	Potential Profit <sup>(2)</sup>
<i>Orchestra Affiliate Shares:</i>				
Legacy Orchestra stockholders – Common Stock received in the Business Combination				
Orchestra Officers and Directors – Common Stock of Legacy Orchestra	245,987	\$ 0.00 <sup>(3)</sup>	\$ 0.00	\$ 1,293,891.62
Series A Preferred Stock of Legacy Orchestra	6,793	\$ 21.51 <sup>(4)</sup>	\$ 146,110.00	*
Series B Preferred Stock of Legacy Orchestra	56,789	\$ 10.73 <sup>(4)</sup>	\$ 609,576.00	*
Series B-1 Preferred Stock of Legacy Orchestra	1,209	\$ 16.13	\$ 19,500.00	*
Series D-1 Preferred Stock of Legacy Orchestra	38,485	\$ 9.09 <sup>(4)</sup>	\$ 349,869.31	*
Series D-2 Preferred Stock of Legacy Orchestra	4,027,996	\$ 10.00	\$ 40,279,629.70	*
Legacy Orchestra stockholders – Common Stock received pursuant to earnout provisions				
	1,696,093	\$ 0.00 <sup>(5)</sup>	\$ 0.00	\$ 8,921,449.18
Medtronic – Common Stock purchased pursuant to the Forward Purchase Agreement				
	999,423	\$ 10.01 <sup>(4)</sup>	\$ 10,004,224.23	*
Orchestra Directors – Common Stock received pursuant to exercise of warrants				
	5,074	\$ 1.08 <sup>(7)</sup>	\$ 5,479.92	\$ 21,209.32
<i>Sponsor and Related Party Shares:</i>				
Sponsor Purchases – HSAC2 ordinary shares converted in the Domestication				
	4,450,000	\$ 1.02 <sup>(6)</sup>	\$ 4,528,750	\$ 18,878,250.00
Entities Affiliated with RTW Investments, LP. – Common Stock received in the Business Combination				
Series B-1 Preferred Stock of Legacy Orchestra	310,000	\$ 16.13	\$ 4,999,951.76	*
Series D-2 Preferred Stock of Legacy Orchestra	2,000,000	\$ 10.00	\$ 20,000,002.20	*
Entities Affiliated with RTW Investments, LP. – Common Stock purchased pursuant to the Backstop Agreement				
	1,808,512	\$ 10.00	\$ 18,085,120.00	*
Entities Affiliated with RTW Investments, LP. – Common Stock purchased pursuant to the Forward Purchase Agreement				
	1,000,000	\$ 10.06	\$ 10,060,000.00	*
Entities Affiliated with RTW Investments, LP. – Common Stock received pursuant to earnout provisions				
	502,133	\$ 0.00 <sup>(5)</sup>	\$ 0.00	\$ 2,641,219.58
Sponsor – HSAC2 Warrant Shares				
	750,000	\$ 11.50 <sup>(7)</sup>	\$ 8,625,000.00	*
Orchestra Officers and Directors – Officer and Director Warrant Shares				
	660,000	\$ 11.50 <sup>(7)</sup>	\$ 7,590,000.00	*
Lenders – shares underlying the Lender Warrants				
	27,707	\$ 7.67 <sup>(7)</sup>	\$ 112,490.42	\$ 33,248.40
Sponsor – HSAC2 Warrant				
	750,000	\$ 1.00 <sup>(8)</sup>	\$ 750,000.00	N/A <sup>(9)</sup>

\* Represents no potential profit per share or a potential loss per share based on illustrative market price.

- (1) The purchase prices prior to the Business Combination have been retroactively restated based on the exchange ratio established in the Merger Agreement.
- (2) Based on the closing price of our Common Stock on the Nasdaq Global Market on March 26, 2024 of \$5.26.
- (3) Represents restricted stock awards granted to directors and executive officers of Legacy Orchestra prior to the Business Combination.
- (4) Represents the weighted average purchase price.
- (5) Represents shares earned pursuant to earnout election agreement, which provided, among other things, that electing Legacy Orchestra stockholders were entitled to receive their Pro Rata Portion (as such term is defined in the Merger Agreement) of 4,000,000 shares of Common Stock if (i) such stockholder agreed to extend their applicable lock-up period from six months to 12 months after the Closing Date and (ii) the volume-weighted average price of the Common Stock was greater than or equal to \$15.00 per share over any 20 trading days within any 30-trading day period that occurred prior to the fifth anniversary of the Closing Date, which was achieved on April 12, 2023.
- (6) 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 450,000 shares in a private placement simultaneously with the HSAC2 IPO at \$10.00 per HSAC2 Ordinary Share (for a total purchase price of \$4,500,000).
- (7) Represents the exercise price of the applicable Warrants.
- (8) The Sponsor purchased, pursuant to a written purchase agreement with HSAC2, an aggregate of 1,500,000 warrants at \$1.00 per warrant (for a total purchase price of \$1,500,000). As part of the Business Combination, 750,000 of these warrants were forfeited immediately prior to the closing of the Business Combination.
- (9) There is no market for the HSAC2 Warrants.

**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 under the heading “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, together with all information contained in this prospectus and any applicable prospectus supplement, and under similar headings in other documents that are incorporated by reference herein or therein. 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 or incorporated by reference into 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.*

## 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 Second Amended and Restated Registration Rights and Lock-Up 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 \$21.0 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. As of the date of this prospectus, the HSAC2 Warrants and the Officer and Director Warrants are “out-of-the money,” which means that the trading price of the shares of our Common Stock underlying the HSAC2 Warrants and the Officer and Director Warrants is below the \$11.50 exercise prices, as applicable (subject to adjustment as described herein), of the Warrants. In addition, 407,841 of the Orchestra Warrants have an exercise price of \$10.22. Thus, a significant majority of the Orchestra Warrants are also “out-of-the money.” For so long as the HSAC2 Warrants, the Officer and Director Warrants and the Orchestra Warrants remain “out-of-the money,” we do not expect warrant holders to exercise those Warrants and therefore any cash proceeds that we may receive in relation to the exercise of such Warrants will be dependent on the trading price of our Common Stock. If the market price for our Common Stock is less than the exercise price of the Warrants, the holders of such Warrants will be unlikely to exercise those Warrants. To the extent that any 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.

## 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 18,586,201 Resale Shares, consisting of:
  - (i) up to 7,077,849 Orchestra Affiliate Shares;
  - (ii) up to 10,070,645 Sponsor and Related Party Shares;
  - (iii) up to 750,000 HSAC2 Warrant Shares;
  - (iv) up to 660,000 Officer and Director Warrant Shares;
  - (v) up to 27,707 shares of Common Stock issuable upon the exercise of the Lender Warrants; and
- (b) the Selling Warrantholder of up to 750,000 HSAC2 Warrants.

Certain of our officers and directors and Medtronic are subject to lock-up agreements covering 6,895,756 shares of common stock (the “Lock-Ups”), including Resale Shares and the Officer and Director Warrants and Common Stock issuable upon exercise of Warrants, pursuant to which our officers and directors and Medtronic have agreed that they will not, without our permission and subject to certain exceptions, among other things, sell or transfer any shares of our capital stock held by such person or any of their affiliates (the “Transfer Restrictions”). The Lock-Ups expire upon the earlier of (i) five calendar days following the date of the publication of certain results of the BACKBEAT pivotal study; *provided*, that in the event the results of the BACKBEAT pivotal study are positive as reasonably determined by Medtronic, the Transfer Restrictions shall continue for an additional five calendar days following the U.S. regulatory approval; *provided, further* that the Transfer Restrictions shall terminate immediately (A) if the BACKBEAT pivotal study is terminated or (B) if the Medtronic Agreement is terminated and (ii) December 16, 2024. All of the securities subject to the Lock-Ups 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 March 22, 2024 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 March 22, 2024 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 35,777,412 shares of our Common Stock issued and outstanding as of March 22, 2024.

Name and Address of Selling Securityholder <sup>(1)</sup>	Beneficial Ownership of Common Stock Prior to the Offering		Warrants Beneficially Owned Prior to the Offering	Number of Shares of Common Stock Being Offered	Warrants Being Offered	Beneficial Ownership of Common Stock After the Offered Shares are Sold		Beneficial Ownership of Warrants After the Offered Warrants are Sold	
	Number of Shares of Common Stock	% of Class				Number of Shares	Percent	Number of Warrants	Percent
HSAC 2 Holdings, LLC <sup>(2)</sup>	5,110,956	14.3%	750,000	5,110,956	750,000	—	—	—	—
RTW Master Fund, Ltd. <sup>(3)</sup>	2,762,705	7.7%	—	2,762,705	—	—	—	—	—
RTW Innovation Master Fund, Ltd. <sup>(4)</sup>	2,263,336	6.3%	—	2,263,336	—	—	—	—	—
RTW Biotech Opportunities Ltd <sup>(5)</sup>	594,604	1.7%	—	594,604	—	—	—	—	—
Ascent Biomedical Ventures II, L.P. <sup>(6)</sup>	1,277,297	3.6%	—	228,073	—	1,049,224	2.9%	—	—
Ascent Biomedical Ventures II NY, LP <sup>(6)</sup>	245,080	*	—	43,761	—	201,319	*	—	—
Ascent Biomedical Ventures Synecor, LP <sup>(6)</sup>	312,406	*	—	55,783	—	256,623	*	—	—
Avenue Venture Opportunities Fund, L.P. <sup>(7)</sup>	37,716	*	25,542	5,542	—	32,174	*	—	—
Avenue Venture Opportunities Fund II, L.P. <sup>(8)</sup>	150,860	*	102,165	22,165	—	128,695	*	—	—
Covidien Group S.a.r.l. <sup>(9)</sup>	5,868,916	16.4%	—	5,868,916	—	—	—	—	—
Perceptive Life Sciences Master Fund <sup>(10)</sup>	2,432,089	6.8%	—	387,191	—	2,044,898	5.7%	—	—
Pedro Granadillo <sup>(11)</sup>	22,261	*	—	22,261	—	—	*	—	—
Stuart Peltz <sup>(12)</sup>	22,261	*	—	22,261	—	—	*	—	—
Michael Brophy <sup>(13)</sup>	22,261	*	—	22,261	—	—	*	—	—
Carsten Boess <sup>(14)</sup>	22,261	*	—	22,261	—	—	*	—	—
David P. Hochman <sup>(15)</sup>	1,040,228	2.8%	225,000	456,823	—	808,405	2.2%	—	—
Darren R. Sherman <sup>(16)</sup>	877,225	2.4%	225,000	308,778	—	793,447	2.2%	—	—
Michael D. Kaswan <sup>(17)</sup>	204,245	*	—	29,029	—	175,216	*	—	—
Yuval Mika <sup>(18)</sup>	335,116	*	50,000	99,572	—	285,544	*	—	—
Fain Living Trust <sup>(19)</sup>	68,904	*	15,000	44,767	—	39,137	*	—	—
Eric Rose <sup>(20)</sup>	44,794	*	15,000	17,168	—	42,626	*	—	—
Jason Aryeh <sup>(21)</sup>	102,121	*	15,000	77,984	—	39,137	*	—	—
Pamela Connealy <sup>(22)</sup>	36,408	*	15,000	19,246	—	32,162	*	—	—
Geoffrey Smith <sup>(23)</sup>	1,870,609	5.2%	—	758	—	1,869,851	5.2%	—	—
George Papandreou, Ph.D. <sup>(24)</sup>	38,631	*	50,000	50,000	—	38,631	*	—	—
Hans-Peter Stoll, M.D., Ph.D. <sup>(25)</sup>	31,386	*	50,000	50,000	—	31,386	*	—	—

\* 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 of Common Stock held and (ii) 750,000 shares of Common Stock that could be acquired upon the exercise of HSAC2 Warrants. According to Amendment No. 2 to Schedule 13D filed by the Sponsor with the SEC on May 5, 2023: (i) Dr. Roderick Wong, M.D. (“Dr. Wong”) is a member of the three-member board of directors of the Sponsor and is also the Managing Partner and Chief Investment Officer of RTW Investments, LP (“RTW Investments”); (ii) Naveen Yalamanchi, M.D. is a member of the Sponsor’s board of directors and is a Partner and Portfolio Manager at RTW Investments; (iii) Alice Lee also

serves on the Reporting Person's board of directors and is Senior Counsel at RTW Investments; (iv) the Sponsor could be deemed to constitute a Section 13(d) group with RTW Investments, RTW Master Fund, Ltd. ("RTW Master Fund"), RTW Innovation Master Fund, Ltd. ("RTW Innovation"), and Dr. Wong and (v) the Sponsor disclaims the existence of a 13(d) group. See footnotes (3) through (5) below for beneficial ownership information relating to Dr. Wong, RTW Investments, RTW Master Fund and RTW Innovation. 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, which is managed by RTW Investments. Dr. Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments. Both he and RTW Investments may be deemed the beneficial owner of the shares held by RTW Investments. The principal business address of RTW Master Fund 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, which is managed by RTW Investments. Dr. Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments. Both he and RTW Investments may be deemed the beneficial owner of the shares held by RTW Innovation. The principal business address of RTW Innovation 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 Ltd., which is managed by RTW Investments. Dr. Wong, the former Chief Executive Officer of HSAC2, serves as the Managing Partner and Chief Investment Officer of RTW Investments. Both he and RTW Investments may be deemed the beneficial owner of the shares held by RTW Biotech Opportunities Ltd. The principal business address of RTW Biotech Opportunities 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 which Avenue I has the right to acquire within 60 days of March 22, 2024 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 securities 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 March 22, 2024 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 securities 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 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. Grandillo. Mr. Grandillo has a principal business address of 40 10<sup>th</sup> 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 10<sup>th</sup> 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 10<sup>th</sup> 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 10<sup>th</sup> Avenue, Floor 7, New York, NY 10014.
- (15) Common Stock beneficially owned prior to the offering (i) consists of (a) 165,498 shares held directly by Mr. Hochman; (b) 62,502 shares held by the DPH 2008 Trust, over which Mr. Hochman has sole voting and dispositive power; (c) 3,823 shares held by the NSH 2008 Family Trust (the “NSH Trust”), over which Mr. Hochman has sole voting and dispositive power; (d) 616,780 shares Mr. Hochman has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly; and (e) 191,625 shares DPH 2008 Trust has the right to acquire within 60 days of March 22, 2024 upon the exercise of options and (ii) does not include 225,000 shares underlying the Officer and Director Warrants held directly by Mr. Hochman. 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 (i) consists of (a) 83,778 shares held directly by Mr. Sherman; and (b) 793,447 shares Mr. Sherman has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 225,000 shares underlying the Officer and Director Warrants held directly by Mr. Sherman. 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) 107,963 shares held directly by Mr. Kaswan; and (ii) 96,282 shares Mr. Kaswan has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly.
- (18) Common Stock beneficially owned prior to the offering (i) consists of (a) 49,572 shares held directly by Mr. Mika; and (b) 285,544 shares Mr. Mika has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 50,000 shares underlying the Officer and Director Warrants held directly by Mr. Mika. 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 (i) consists of (a) 29,767 shares held by the Fain Living Trust (the “Fain Trust”), over which Mr. Fain has sole voting and dispositive power; and (b) 39,137 shares the Fain Trust has the right to acquire within 60 days of March 22, 2024 upon the exercise of options it holds and (ii) does not include 15,000 shares underlying the Officer and Director Warrants held directly by Mr. Fain. 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 (i) consists of (a) 2,169 shares held directly by Mr. Rose; and (b) 42,625 shares Mr. Rose has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 15,000 shares underlying the Officer and Director Warrants held directly by Mr. Rose. 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 (i) consists of (a) 62,984 shares held directly by

- Mr. Aryeh; and (b) 39,137 shares Mr. Aryeh has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 15,000 shares underlying the Officer and Director Warrants held directly by Mr. Aryeh. 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 (i) consists of (a) 4,246 shares held directly by Ms. Connealy; and (b) 32,162 shares Ms. Connealy has the right to acquire within 60 days of March 22, 2024 upon the exercise of options she holds directly and (ii) does not include 15,000 shares underlying the Officer and Director Warrants held directly by Ms. Connealy. 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) 2,502 shares held directly by Mr. Smith; (ii) 33,324 shares Mr. Smith has the right to acquire within 60 days of March 22, 2024 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.
- (24) Common Stock beneficially owned prior to the offering (i) consists of 38,631 shares Mr. Papandreou has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 50,000 shares underlying the Officer and Director Warrants held directly by Mr. Papandreou. 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 (i) consists of 31,386 shares Mr. Stoll has the right to acquire within 60 days of March 22, 2024 upon the exercise of options he holds directly and (ii) does not include 50,000 shares underlying the Officer and Director Warrants held directly by Mr. Stoll. 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.

## PLAN OF DISTRIBUTION

We are registering the issuance by us of up to an aggregate of 1,917,841 Warrant Shares, consisting of up to:

- (a) 750,000 HSAC2 Warrant Shares;
- (b) 660,000 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 18,586,201 Resale Shares, consisting of:
  - (i) up to 7,077,849 Orchestra Affiliate Shares;
  - (ii) up to 10,070,645 Sponsor and Related Party Shares;
  - (iii) up to 750,000 HSAC2 Warrant Shares;
  - (iv) up to 660,000 Officer and Director Warrant Shares;
  - (v) up to 27,707 shares of Common Stock issuable upon the exercise of the Lender Warrants; 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 overallocments 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 USRPHC 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 our certificate of incorporation (the “Charter”), the our bylaws (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 Delaware General Corporation Law (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 March 22, 2024, there were 35,777,412 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 March 22, 2024, there are outstanding warrants to acquire up to an aggregate of 1,945,548 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. However, 90,000 of the initial 750,000 Officer and Director Warrants were forfeited in connection with the departure of Orchestra's former Chief Financial Officer and one Orchestra director. Accordingly, there are currently 660,000 Officer and Director Warrants outstanding. 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 Capital Corp. ("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 became exercisable one year after the closing of the Business Combination.

*Warrants Issued to Designees of Aegis 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 became 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 with Avenue I and Avenue II (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 up to 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.

#### **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 18,458,494 Resale Shares of Common Stock (including up to 1,310,000 shares of Common Stock issuable upon exercise of the Warrants). 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 statement was required to be filed by no later than May 26, 2023. However, the Company and the requisite holders of registrable securities waived the requirement to file a registration statement until October 23, 2023. The registration statement was filed on October 10, 2023. However, on November 21, 2023, the Company and the requisite holders of registrable securities entered into the Second Amended and Restated Registration Rights Agreement (the “Second A&R RRA”), which amended and restated the Amended and Restated Registration Rights Agreement to provide that the registration statement of which this prospectus is a part did not have to be amended until earlier the earlier of (i) April 1, 2024 or (ii) fifteen (15) business days after the Company files its Annual Report on Form 10-K for the year ended December 31, 2023. In addition, pursuant to the Second A&R RRA and subject to certain limited exceptions, we are required to use commercially reasonable efforts 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 Second A&R RRA 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 Second A&R RRA

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 Second A&R RRA contains customary indemnification provisions.

#### **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***

The size of our Board is currently set at 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 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.

### **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. appearing in Orchestra BioMed Holdings, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2023, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference 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-3, 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](http://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.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus or any applicable prospectus supplement is considered to be part of this prospectus and any prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus and any applicable prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus, any prospectus supplement or in any document previously incorporated by reference herein or therein have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than information deemed furnished and not filed in accordance with SEC rules, including Items 2.02 and 7.01 of Form 8-K) until the offering of the securities offered hereby is terminated or completed:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2023, filed with the SEC on March 27, 2024; and
- the description of our Common Stock contained in [Exhibit 4.16](#) to our Annual Report on Form 10-K for the fiscal year ended December 31, 2023 filed with the SEC on March 27, 2024, including any amendment or reports filed for the purpose of updating such description.

In addition, all reports and other documents we may file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the registration statement of which this prospectus forms a part, including prior to effectiveness of such registration statement, shall be deemed to be incorporated by reference into this prospectus.

We are not, however, incorporating by reference any documents or portions thereof that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements. Any such statement so modified or superseded shall not be deemed to constitute a part of this prospectus, except as so modified or superseded.

You may request a free copy of these filings (other than an exhibit to a filing unless that exhibit is specifically incorporated by reference into that filing) by writing or telephoning us as follows:

Orchestra BioMed Holdings, Inc.  
150 Union Square Drive  
New Hope, PA 18938  
212-862-5797

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. 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
<b>Total</b>	<b><u>\$413,463</u></b>

**Item 15. 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 16. Exhibits.

The following exhibits are filed as part of this registration statement:

Exhibit	Description
2.1#	<a href="#"><u>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).</u></a>
2.2#	<a href="#"><u>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).</u></a>
2.3#	<a href="#"><u>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).</u></a>
4.1	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.2	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.3	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.4	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>

Exhibit	Description
4.5	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.6	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.7	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.8	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.9	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.10	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.11	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.12	<a href="#"><u>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), filed with the SEC on December 12, 2022).</u></a>
4.13	<a href="#"><u>Amended &amp; 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).</u></a>
4.14	<a href="#"><u>Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund, L.P., dated October 6, 2023 (incorporated by reference to Exhibit 4.14 to the Company's Form S-1 (File No. 333-274924), filed with the SEC on October 10, 2023).</u></a>
4.15	<a href="#"><u>Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund II, L.P., dated October 6, 2023 (incorporated by reference to Exhibit 4.15 to the Company's Form S-1 (File No. 333-274924), filed with the SEC on October 10, 2023).</u></a>
5.1+	<a href="#"><u>Opinion of Paul Hastings LLP.</u></a>
23.1+	<a href="#"><u>Consent of Ernst &amp; Young LLP, independent registered public accounting firm of Orchestra BioMed Holdings, Inc.</u></a>
23.2+	<a href="#"><u>Consent of Paul Hastings LLP (included in Exhibit 5.1).</u></a>
24.1+	<a href="#"><u>Power of Attorney (included on the signature page to this Registration Statement).</u></a>
107*	<a href="#"><u>Calculation of Filing Fee Table.</u></a>

\* Previously filed.

+ Filed herewith.

# 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.**

- (a) 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 (the “Securities Act”);
    - (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 SEC 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:
  - (i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
  - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) (§ 230.424(b)(2), (b)(5), or (b)(7) of this chapter) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) (§ 230.415(a)(1)(i), (vii), or (x) of this chapter) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. 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 effective date, 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 effective date.

- (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, 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.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement 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.
- (c) Insofar as indemnification for liabilities arising under the Securities Act 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 certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and 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 27th day of March, 2024.

**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.

<u>Name</u>	<u>Title</u>	<u>Date</u>
/s/ David P. Hochman David P. Hochman	Chief Executive Officer, Chairperson and Director <i>(Principal Executive Officer)</i>	March 27, 2024
/s/ Andrew L. Taylor Andrew L. Taylor	Chief Financial Officer <i>(Principal Financial Officer)</i>	March 27, 2024
/s/ Joshua Aiello Joshua Aiello	Corporate Controller <i>(Principal Accounting Officer)</i>	March 27, 2024
/s/ Jason Aryeh Jason Aryeh	Director	March 27, 2024
/s/ Pamela A. Connealy Pamela A. Connealy	Director	March 27, 2024
/s/ Eric S. Fain, M.D. Eric S. Fain, M.D.	Director	March 27, 2024
/s/ David Pacitti David Pacitti	Director	March 27, 2024
/s/ Eric A. Rose, M.D. Eric A. Rose, M.D.	Director	March 27, 2024
/s/ Darren R. Sherman Darren R. Sherman	President, Chief Operating Officer and Director	March 27, 2024



March 27, 2024

Orchestra BioMed Holdings, Inc.  
150 Union Square Drive  
New Hope, Pennsylvania 18938

Re: Orchestra BioMed Holdings, Inc. Pre-Effective Amendment No. 1 to Form S-1 on Form S-3 Registration Statement

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 a Pre-Effective Amendment No. 1 on Form S-3 to the Registration Statement on Form S-1 of the Company originally filed with the Commission on October 10, 2023 (File No. 333-274924) (as amended, the "**Registration Statement**"), including a related prospectus filed with the Registration Statement (the "**Prospectus**"), relating to (a) the issuance of up to 1,917,841 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 18,586,201 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 660,000 shares of Common Stock (the "**Officer and Director Warrant Shares**") upon the exercise of 660,000 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 18,586,201 shares of Common Stock (collectively, the "**Resale Shares**"), consisting of:
  - a. up to 7,077,849 shares of Common Stock issued to certain stockholders of the Company;
  - b. up to 10,070,645 shares of Common Stock held by the Sponsor and certain entities related to the Sponsor;

Paul Hastings LLP | 200 Park Avenue | New York, NY 10166  
t: +1.212.318.6000 | www.paulhastings.com

Orchestra BioMed Holdings, Inc.

March 27, 2024

Page 2

- c. up to 750,000 HSAC2 Warrant Shares;
- d. up to 660,000 Officer and Director Warrant Shares; and
- e. 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 March 26, 2024 (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 March 21, 2024 (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.

---

Orchestra BioMed Holdings, Inc.

March 27, 2024

Page 3

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.

---

Orchestra BioMed Holdings, Inc.

March 27, 2024

Page 4

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

---

**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated March 27, 2024 in Pre-Effective Amendment No.1 to Form S-1 on Form S-3 (Form S-3 No. 333-274924) and related Prospectus of Orchestra BioMed Holdings, Inc. for the registration of up to 18,586,201 shares of common stock, up to 1,917,841 shares of common stock issuable upon the exercise of warrants, and up to 750,000 warrants.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania  
March 27, 2024

---