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

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): November 12, 2025

ORCHESTRA BIOMED HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-39421**	**92-2038755**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

150 Union Square Drive
New Hope, Pennsylvania 18938
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (215) 862-5797

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.0001 per share	**OBIO**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On November 12, 2025, Orchestra BioMed Holdings, Inc. (the "Company") held a conference call via a live audio and video webcast (the "Conference Call"), to discuss certain significant business updates with respect to clinical, strategic and financing developments of the Company. A copy of the transcript of the Conference Call (the "Transcript") and the investor presentation presented during the Conference Call (the "Investor Presentation"), are attached to this Current Report on Form 8-K ("Current Report") as Exhibit 99.1 and as Exhibit 99.2, respectively, and are incorporated herein by reference solely for purposes of this Item 7.01 disclosure.

The information in Item 7.01 of this Current Report, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of such section. The information in Item 7.01 of this Current Report, including Exhibit 99.1 and Exhibit 99.2, shall not be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any incorporation by reference language in any such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Transcript of the Conference Call held on November 12, 2025.
99.2	Investor Presentation presented during the Conference Call held on November 12, 2025
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ORCHESTRA BIOMED HOLDINGS, INC.

By: /s/ Andrew Taylor
Name: Andrew Taylor
Title: Chief Financial Officer

Date: November 13, 2025

Orchestra BioMed

Third Quarter 2025 Corporate Update Conference Call

12 November 2025

C O R P O R A T E P A R T I C I P A N T S

Kelsey Kirk-Ellis, *Director, Corporate Communications*

David Hochman, *Chairman, Chief Executive Officer and Founder*

Andrew Taylor, *Chief Financial Officer*

C O N F E R E N C E C A L L P A R T I C I P A N T S

Matthew O'Brien, *Piper Sandler*

Matthew Miksic, *Barclays*

Marie Thibault, *BTIG*

Anderson Schock, *B. Riley Securities*

Josh Jennings, *TD Cowen*

Eduardo for Yi Chen, *H.C. Wainwright*

P R E S E N T A T I O N

Operator

Greetings. Welcome to Orchestra Bio's Third Quarter 2025 Corporate Update Call.

At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation. If anyone should require operator assistance during the conference, please press star, zero on your telephone keypad.

Please note, this conference is being recorded.

I will now turn the conference over to Kelsey Kirk-Ellis, Director of Corporate Communications. Thank you. You may begin.

Kelsey Kirk-Ellis

Starting on Slide 2, before the call begins we would like to advise you that management will be making forward-looking statements in their comments concerning expectations regarding certain transactions, as well as Management's expectations regarding our financial condition and cash runway. These forward-looking statements are based on Management's current expectations and are subject to risks and uncertainties that could cause actual results to differ materially, including the risks listed under the heading Item 1A Risk Factors in our Form 10-K for the year ended December 31, 2024, and in our quarterly report on Form 10-Q for the quarter ended March 31, 2025.

Management undertakes no obligation to update its forward-looking statements to reflect subsequent events or circumstances, and you should not assume that the comments made today are valid in the future.

I'm now pleased to introduce David Hochman.

David Hochman

Good morning and thank you for joining us today. My name is David Hochman and I am the Chairman and CEO of Orchestra BioMed. Before we begin, I'd like to note that, while today's update follows the recent release of our third quarter financial results, this call is not intended to review financial performance or provide earnings-related commentary, nor are we necessarily going to provide a business update call like this to coincide with all future quarterly financial filings. As we are doing today, we will host business updates when we have significant developments for which we believe providing additional perspective to shareholders and investors is beneficial.

Now moving to Slide 3.

Orchestra BioMed was founded to pursue a partnership-enabled business model. Our goal is to accelerate high-impact medical device innovations to physicians and patients through strategic partnerships with global market leaders. By focusing our efforts on product development through pivotal trial data and aligning our interests with established global market leaders, our goal is to benefit patients and physicians while yielding exceptional profitability for our shareholders.

We built the Company around two flagship programs, AVIM Therapy and Virtue SAB, that address targeted unmet needs within hypertensive heart disease and artery disease, two of the most significant medical problems in the world. The opportunities for our therapies both represent multi-billion dollar markets within two of the most established fields of interventional medicine, cardiac rhythm management and interventional cardiology.

Today, I am proud to say we are enrolling patients in pivotal IDE trials for both our therapies for their lead indications. These trials are specifically designed to generate clinical data to support regulatory approvals and commercial adoption of our therapies. We are well-funded and well-organized to drive these studies through completion of enrollment and in the case of AVIM therapy, primary endpoint results.

Our goal today is to highlight and provide additional context with respect to our significant achievements over the last several months.

During that period, we raised nearly $150 million in capital and capital commitments, strengthened our collaboration with Medtronic, entered into a new right of first refusal agreement with Terumo that replaces our prior agreement, entered into a new strategic capital relationship with Ligand, secured FDA Breakthrough Device Designation for AVIM Therapy, significantly enhanced the protocol for our BACKBEAT global pivotal trial, and launched enrollment of our U.S. pivotal coronary trial for Virtue SAB.

We are very proud of these accomplishments, and I want to recognize and congratulate the entire Orchestra BioMed team for their contributions to these achievements.

In today's call, I will review each of them briefly and explain how we are now optimally positioned to achieve our next major objectives of completing enrollment of both our pivotal trials and advancing the primary endpoint readout.

Now let's move to Slide 4.

Let's start by reviewing how we secured nearly $150 million in financing over the last few months.

On August 4, we announced the completion of a multi-component strategic-led financing, which, with the subsequent exercise of the equity financing greenshoe, generated total gross proceeds of $117.6 million. I want to take some time to talk about the different elements of this financing, which was principally led by our existing AVIM therapy strategic collaborator, Medtronic, and a new strategic capital partner, Ligand. It's important to review the scope and structure of each transaction so investors can understand how this provided critical capital in a way that protects shareholder value, limits equity dilution, reaffirms the alignment we already have with Medtronic, and brought, in the form of Ligand's investment, a long-term minded and outstanding new strategic investor into the fold.

There were three components to the overall financing. Two of these were the $55 million in capital committed to Orchestra from non-dilutive transactions with Medtronic and Ligand. The third was over $62 million that came in as equity investments with Medtronic and Ligand acting as key lead equity investors as well. I'll first detail the strategic investments, then move on to the equity structure.

In terms of the non-equity strategic components, Medtronic is, as you are likely already aware, our strategic collaborator for the development and commercialization of AVIM therapy for the treatment of uncontrolled hypertension in patients indicated for a pacemaker. Medtronic also has the right of first negotiation to expand our collaboration to the broader hypertension population. We are entitled to royalties on the future sales of AVIM-enabled devices that Medtronic commercializes.

Medtronic committed $31.6 million in additional capital to the Company; $11.6 million came in as additional equity in a private placement structure, bringing Medtronic's total equity investment in Orchestra BioMed to nearly $62 million and their total ownership percentage to approximately 18%. Medtronic also committed an additional $20 million to the Company in the form of a long-term convertible note instrument. That capital is fully committed and expected to be received in April 2026. Importantly, this note will convert into a revenue share credit structure upon FDA approval of AVIM therapy. Ultimately, we will credit back to Medtronic 15% of the royalties we receive from them for sales of AVIM therapy-enabled devices up to a cap of $40 million. We believe this structure reflects Medtronic's enthusiasm for the clinical and commercial potential of AVIM therapy.

We are very excited to now have Ligand as a new strategic financial partner. Ligand is a biopharmaceutical company that invests in the groundbreaking medicines of today and tomorrow. Ligand funds the clinical development and commercialization of high-value programs that can improve and extend lives around the world. Their business model focuses on generating revenue through royalties, licensing fees, and milestone payments from a broad portfolio of partnered programs. In August, Ligand committed $35 million to purchase a stake in Orchestra's future royalty-based cash flows from AVIM therapy and Virtue SAB. Essentially, Ligand purchased a royalty on our future royalties. Ligand funded the first $20 million tranche and will provide the remaining $15 million at the end of April next year, subject to customary conditions.

Ligand also joined Medtronic and purchased $5 million of equity in a parallel private placement, bringing their total investment commitment to $40 million. We believe Ligand's strategic investment commitment to Orchestra is based on their confidence, following substantial due diligence, that both AVIM therapy and Virtue SAB can generate significant royalty cash flows to Orchestra BioMed in the future. Ligand's long-term return profile assumes that we and our partners will successfully bring our therapies to market and generate strong future cash flows.

The last component of our major financing announcement in August was the simultaneous completion of our first underwritten public equity offering, for which Piper Sandler and TD Cowen acted as joint bookrunners. This financing was oversubscribed and the underwriters exercised their option to purchase additional shares. Our underwritten public offering included significant participation from large existing shareholders and generated total gross proceeds of $46 million.

Combined with the $16.6 million in gross proceeds from the parallel PIPE with Medtronic and Ligand, we brought in a total of $62.6 million in equity proceeds. Added to our $55 million in strategic commitments, our August financing event secured a total of $117.6 million.

On October 28th, we announced our new strategic agreements with Terumo, which generated an additional $30 million in proceeds to Orchestra. This capital came in the form of a $10 million payment in exchange for granting Terumo a right of first refusal related to Virtue SAB in the coronary market, as well as a $20 million purchase of non-voting preferred stock. Notably, the preferred stock cannot convert to common until we disclose the primary endpoint from the Virtue Trial to Terumo, and our stock is traded above $15 per share subsequent to such disclosure. Further, the conversion price is the higher of $12 per share, or a 20% discount from where the stock is trading at the time of conversion. The preferred stock can also convert into common in the event of certain change of control transactions. We view these terms as quite favorable to our current shareholders.

The combination of these multiple strategic and equity financings, which with the additional capital from Terumo add up to an aggregate of $147.6 million, materially strengthen our balance sheet and extend our cash runway into the fourth quarter of 2027. Most importantly, they give us the resources to pursue aggressive execution of enrollment in both of our pivotal trials and other key operational initiatives. We are proud of the creative and resourceful approach we took to secure this capital while limiting equity dilution and protecting long-term value creation opportunities for our shareholders.

Let's talk about our new Terumo rights agreement in more detail on Slide 5.

We're very pleased to have reached positive new alignment with Terumo. Our new agreement, for which we received $10 million of the additional $30 million from Terumo, provides Terumo with a right of first refusal with respect to certain strategic transactions relating to Virtue SAB in the field of coronary artery disease treatment. This new arrangement supersedes and replaces our prior, now terminated, distribution agreement, for which Terumo had already paid us $30 million and invested $5 million in equity. From our perspective, this new agreement provides clarity, additional capital on favorable terms, and broad strategic optionality to realize the full potential of our Virtue SAB technology.

The Terumo right of first refusal is in place until 90 days after we disclose to Terumo the primary endpoint data from the Virtue Trial. While in effect, Orchestra is free to engage other strategic parties and explore a wide variety of partnership or strategic transaction structures, including M&A. If we decide to pursue an attractive transaction for Virtue SAB in the coronary field with a third party, we will notify Terumo and they will have 30 days to exercise their right of first refusal, and if the right is exercised, another 90 days to complete a transaction on substantially the same terms offered by the third party.

Importantly, Orchestra BioMed retains full operational and execution control of the Virtue Trial. We also have full developmental rights to our Virtue SAB asset, including rights to Virtue SAB and SirolimusEFR in coronary artery disease, peripheral artery disease, other vascular indications, as well as potential future indications where we think our technology can have value. As Ghada Farah, president of Terumo Interventional Systems, stated in our press release, Terumo is, and I quote, "very pleased to enter into a new strategic agreement with Orchestra BioMed that reflects the significant potential for Virtue SAB in the treatment of coronary artery disease. We believe it aligns the objectives of both companies, and we wish Orchestra BioMed great success as they enroll patients in the Virtue Trial," end quote.

Let's talk about Virtue SAB and the Virtue Trial in more detail, and let's move to Slide 6.

Orchestra BioMed strongly believes that Virtue SAB and SirolimusEFR, its key enabling pharmaceutical component, can become a best-in-class treatment for atherosclerotic artery disease. As such, we were thrilled to announce the day before we announced the new Terumo agreement that we had completed the initial patient enrollments in the Virtue Trial. The Virtue Trial is a pivotal U.S. trial that will randomize Virtue SAB against Boston Scientific's AGENT paclitaxel-coated balloon, currently the only drug-coated balloon approved by the FDA for a coronary indication. The focus of this trial is coronary ISR, or in-stent restenosis.

Coronary ISR is a difficult-to-treat complication of coronary stenting where patients that have been previously treated with a permanent coronary stent now require additional treatment at the same location.

The treatment of coronary artery disease is currently undergoing a paradigm shift towards leave-nothing-behind treatment strategies that aim to leverage drug-delivery balloon treatments that do not leave metal stents permanently in the artery. This paradigm shift is gaining clinical momentum worldwide in an established global market for coronary artery treatment that we estimate is valued at approximately $7.5 billion annually.

This category of devices is comprised entirely, with the exception of our own Virtue SAB, of drug-coated balloons, standard angioplasty balloons coated with anti-restenotic drugs such as paclitaxel and sirolimus. The AGENT paclitaxel-coated balloon, the first such drug-coated balloon to be approved in the U.S. for coronary use, has seen rapid commercial uptake since its launch late last year. This commercial adoption has been supported by significant add-on reimbursement for drug-delivery balloons that is enabling average selling prices above $6,000.

Attractive enhanced U.S. reimbursement that we believe is applicable to the entire drug-delivery balloon category is converging with a growing body of clinical evidence. This includes two significant late-breaking drug-coated balloon clinical studies reported at the TCT conference in San Francisco a couple of weeks ago that further support the idea that drug-delivery balloons can provide equivalent clinical outcomes for patients without the risks and burdens of permanent stent implants.

Drug-coated balloons all come with similar challenges, regardless of whether they are coated with paclitaxel or sirolimus. First, there is a limited amount of drug that can be coated on the surface of the balloon. Second, all coated balloons lose a significant portion of their surface coating and drug during transit through the arteries to the site of treatment prior to balloon inflation; as much as 80% of the drug according to one study.

These devices lose more drug during balloon inflation, so ultimately there is a very limited amount of drug that gets delivered to the treatment site.

Furthermore, the coatings are inherently fragile as they are designed to come off the balloon upon inflation. Published data shows that all drug-coated balloons produce large micron-sized particulates that can form emboli and produce unwanted downstream effects. Because of these challenges, physicians are encouraged to navigate drug-coated balloons very quickly to the treatment site and deploy them promptly.

Let's look at Slide 7.

We designed Virtue SAB to overcome the limitations of drug-coated balloons in order to optimize the impact of arterial drug delivery during interventional procedures and help realize the full potential of leave-nothing-behind treatment strategies.

The core enabling technology behind Virtue SAB is our proprietary SirolimusEFR, or extended focal release formulation. Sirolimus is a proven gold standard drug class used now on all drug-eluting stents that support arterial healing post-interventional procedure and prevent restenosis or reclogging of the artery. SirolimusEFR is a unique and proprietary nano-encapsulated formulation designed to enable optimal arterial uptake. We paired our proprietary drug formulation with our novel patented microporous balloon delivery system. This drug-device combination is designed to deliver a large liquid dose of SirolimusEFR directly to the arterial treatment site without needing a permanent stent implant or a fragile balloon surface coating. Virtue stands out as the only non-coated drug delivery balloon system capable of also performing angioplasty.

Virtue SAB is fundamentally different than drug-coated balloons by design. Our SirolimusEFR formulation is manufactured separately and not coated on the balloon surface. A measured dose is prepared and loaded at the back of the catheter, matched precisely with the length and diameter of the chosen balloon device. The drug is protected through the entire procedure within the catheter, so no drug is lost in transit. Further, Virtue has passed all FDA particulate testing and has been shown not to produce large particulates. It allows physicians to take their time to navigate and position the device carefully. Only when they decide to initiate balloon inflation does drug formulation start to be delivered to the target lesion, and they can visibly see the entire dose get delivered.

Virtue is designed to deliver a large liquid dose of SirolimusEFR, which is specifically engineered to be taken up by the arterial tissue, form a local depot of drug which then gets released over the entire time of the critical healing period post-procedure. Published preclinical data involving over 750 treated artery segments show that the dose of sirolimus Virtue delivers to the target arterial site is maintained well above the established target tissue concentration of 1 nanogram per milligram of tissue through the entire critical healing period, well exceeding published tissue concentrations of proven commercial drug-leading stents, as well as Sirolimus-coated balloons that are currently under clinical investigation in the U.S.

We move to Slide 8.

Clinical results from the SABRE pilot multicenter clinical study of Virtue SAB and coronary ISR further support our confidence in our innovation. This study showed that Virtue had a best-in-class outcome of 2.8% target lesion failure and single-layer restenosis at the one-year primary endpoint follow-up.

Target lesion failure is a composite safety and efficacy endpoint that assesses whether a patient had a major adverse cardiac event or needed retreatment, known as target lesion revascularization, or TLR. The best result is the lowest possible number.

The goal of leave-nothing-behind treatment strategies is to maintain effective treatment results long-term, and we were delighted to see that Virtue SAB-treated patients needed zero revascularization interventions from one year through three years follow-up.

Let's look at Slide 9.

In the same type of lesions—single-layer restenosis—the AGENT balloon resulted in a 13.5% target lesion failure rate in its IDE study. Notably, the two-year data showed an overall increase of more than 50% in target lesion failure for AGENT compared to one-year results, meaning that a number of patients had major adverse events or needed retreatment after the first year.

In the recently reported clinical results from Cordis' SELUTION-SLR IDE study in coronary ISR, that product—a sirolimus-coated balloon—demonstrated a similar 13.2% TLF rate in single-layer restenosis at one-year follow-up, almost identical to the AGENT results. Looking at these results, we see clear potential for Virtue SAB to deliver improved clinical outcomes.

Let's look at Slide 10 in the Virtue Trial.

The Virtue Trial is designed to provide the data necessary to gain regulatory approval for Virtue SAB, as well as showcase our fundamentally different, and we believe, superior approach to arterial drug delivery. The primary endpoint is TLF non-inferiority at one-year follow-up. We are very confident that Virtue SAB can achieve statistical non-inferiority and hope to also further showcase the advantages of the product with better TLF performance. We will enroll 740 patients at up to 75 centers in the United States. Our team will be busy activating centers well into next year and driving effective patient enrollment.

We believe Virtue SAB is a very exciting pivotal-stage asset that offers a substantial future value creation opportunity, which we are driving toward from a position of financial, operational, and strategic strength.

Let's go to Slide 11 and look more closely at the AVIM therapy program.

Looking at this program and our BACKBEAT global pivotal study, 2025 has been an eventful and highly productive year. AVIM, or atrioventricular interval modulation therapy, is a novel treatment for hypertensive heart disease delivered entirely as proprietary programming to a dual chamber pacemaker. The therapy is designed to reduce blood pressure immediately and substantially, and to maintain lower blood pressures for years, as we have demonstrated with our prior pilot clinical study results.

AVIM therapy is protected by a very strong, carefully constructed patent estate that includes over 120 issued patents related to the treatment of hypertension alone. We have additional issued patents related to other indications such as heart failure.

In addition to Medtronic's further $31.6 million strategic investment commitment that I detailed earlier, we announced several key AVIM therapy program updates this year. First, in conjunction with the additional investment, we also expanded the scope of our strategic collaboration with Medtronic for the potential integration of AVIM therapy into future leadless pacing technology. Second, we started implementing an additional substantial protocol update to our ongoing BACKBEAT study that streamlines enrollment and significantly broadens patient eligibility across participating sites. The rollout of this improved protocol is nearly complete. We've already seen meaningful impact on site activity and enrollment. We continue to target enrollment completion next year.

Let's look at Slide 12.

This progress builds on strong momentum from the second quarter when we announced the FDA-granted Breakthrough Device Designation for AVIM therapy for the treatment of patients with uncontrolled hypertension despite medication who also have increased cardiovascular risk and preserved ejection fraction. Importantly, this Breakthrough Device Designation covers both our initial beachhead market of patients with hypertension who already have or require a pacemaker—an estimated 300,000 patients annually in the U.S.—as well as a broader population of more than 7.7 million patients that we estimate fall under the Breakthrough indication. These patients are typically older and at higher risk of isolated systolic hypertension, diastolic dysfunction, and heart failure with an elevated systolic blood pressure.

Clinical data from prior pilot studies has shown the potential utility of AVIM therapy in treating all of these comorbid conditions. Breakthrough Designation underscores the significant unmet need for controlling blood pressure in these higher-risk patients and the commercial opportunity for AVIM therapy to address high-risk hypertensive heart disease, an aggregate global annual market opportunity we estimate exceeds $17 billion.

Move to Slide 13.

In addition to these regulatory and strategic achievements, we achieved a number of additional clinical milestones for the AVIM therapy program with peer-reviewed data publications and clinical conference presentations. *The Journal of the American College of Cardiology: Advances* published MODERATO II study data showing AVIM therapy significantly lowered systolic blood pressure and improved key measures of ventricular function in patients with diastolic dysfunction. These results showcase AVIM therapy's potential to slow the progression to heart failure with preserved ejection fraction, a significant patient population with unmet treatment needs.

JACC: Clinical Electrophysiology published our pressure volume loop analysis demonstrating short- and long-term hemodynamic effects of AVIM therapy in hypertensive patients fitting the profile of patients targeted for the BACKBEAT study. The analysis showed AVIM therapy significantly reduced systolic blood pressure, improved left ventricular end-diastolic and end-systolic volumes, and reduced total peripheral resistance without compromising cardiac output. These AVIM therapy results were consistent using ventricular lead placements in conventional as well as conduction system locations. Conduction system pacing, primarily targeting the left bundle branch area, is being widely adopted now in clinical practice and promises to reduce certain key risks historically associated with active ventricular patients.

Now moving to Slide 14.

At HRX Live 2025, we presented new clinical data from long-term follow-up of patients treated with AVIM therapy that show, one, blood pressure reduction was sustained for an average of over 3.5 years after activation; that, two, the effect was reversible with no observed rebound hypertension upon deactivation of treatment; and that, three, the effect was reproducible upon reactivation following a washout period. This treatment durability and flexibility underscores AVIM therapy's clinical utility and future potential as a programmable device-based treatment that can drive substantial and sustained blood pressure reductions.

Now moving to Slide 15, I'd like to summarize.

2025 has clearly been a successful and eventful year for Orchestra BioMed to date, with recent developments positioning us to operate on all cylinders for both of our pivotal stage high-impact programs.

Our pivotal trials are both underway and actively enrolling. We are very pleased to achieve a favorable realignment with Terumo, expanded our collaboration with Medtronic, and have secured significant additional capital on terms we believe are attractive for shareholders through transactions driven by our strategic investors, including Ligand, our strategic capital partner.

The result of these financing efforts is that we are very well capitalized to achieve key clinical and regulatory milestones. We expect 2026 will be a landmark year for Orchestra BioMed, with target completion of enrollment in the BACKBEAT study and primary endpoint results data to follow thereafter, given that the primary efficacy and safety endpoints are measured at three months follow-up. Active enrollment of the Virtue Trial is now underway, with the completion of enrollment targeted in mid-2027.

As noted at the start of this update, we won't review this quarter's financials, but they are available in our Form 10-Q filing and press release.

I will note that our cash balance at the end of the quarter was $96 million, not including $30 million we received from Terumo on November 7, as well as $35 million in committed capital we expect to receive from Medtronic and Ligand in the second quarter of next year.

Thank you all for joining this session and for your continued interest in Orchestra BioMed. We are now happy to open the line for questions. For Q&A, I'm very pleased to be joined by our CFO, Andrew Taylor.

Operator

Thank you. We will now be conducting a question-and-answer session. If you would like to ask a question, please press star, one on your telephone keypad. A confirmation tone will indicate your line is in the question queue. You may press star, two if you would like to remove your question from the queue. For participants using speaker equipment, it may be necessary to pick up your handset before pressing the star keys.

Our first question is from Matthew O'Brien with Piper Sandler. Please proceed.

Matthew O’Brien

Good morning. Thanks for taking my questions. Dave, maybe just talk a little bit about the enrollment with respect to AVIM. I think you said to expect it to be complete by next year. Is that something that you could see kind of middle of next year and then once it is finished enrolling, maybe talk a little bit about next steps after that through full commercialization? And then I have a follow-up.

David Hochman

Sure. Thanks, Matt. We still have provided guidance of mid-next year. We'll hopefully be able to refine that as we approach our 10-K and obviously be able to give it a little more granular.

We are excited about the progress we've been making, particularly since implementing the new protocol. As I noted in the call, the primary endpoints, both for efficacy and safety, are measured at three-month follow-ups. Obviously it will take us a little more time than just three months to analyze and scrub the data from the electronic database and then find the appropriate forum both for sharing top line data and then probably more detailed data. There is blinded follow-up through 12 months.

Our hope would be, and Medtronic is responsible ultimately for the regulatory submission of what will be a PMA supplement. We believe the primary endpoint is going to be critical to the submission, along with the (inaudible) data from the commercial device platform, which is well down the path of development that's been being developed in parallel to executing the study.

The FDA may likely want to see some of the 12-month data before approval, but the hope would be that submission could be made in 2027. Obviously, promptly after data is available that the data and the filing can be reviewed and perhaps then you're waiting for the 12-month data for full approval.

Our models really expect that Medtronic can start U.S. commercialization hopefully early in 2028 and global commercialization over the course of 2028.

Matthew O’Brien

Got it. Then similarly, just moving over to Virtue and that study, I would imagine that will probably enroll faster than AVIM, so just maybe talk a little bit about what to expect in terms of maybe pace of enrollment. I know you don't want to give a timeframe yet as far as when you could be finished there, but just maybe pace of enrollment there. Then I do have one more if I can sneak it in for Andrew.

David Hochman

When we announced the trial, we did announce target enrollment also in mid, in this case, 2027.

We do think that the trial, it's a trial format that is familiar to our participating sites. Many of the sites that we're working with or that will join the study have participated in either the AGENT study or the SELUTION study or other drug-coated balloon studies that are now being executed. It's a fairly familiar format.

We also think that enrollment will be helped by the fact that we're randomizing against AGENT, which is approved, and we're doing everything we can to support the sites, so really there's no tradeoffs for patients. They're either getting the most recent approved drug-coated balloon or what we believe is such an exciting investigational device in terms of Virtue.

There's still a lot of work to do, Matt, in terms of site activations, and as I noted in the call, we'll be activating sites well into next year, gearing them up, but hopefully getting those sites to a state of active enrollment very quickly.

That said, we're still trying to be thoughtful about our target enrollment and we'll provide more perspective and, once again, more granular information on enrollment as we progress through the ramp-up of the study over the course of next year. The data in that case is a 12-month TLF endpoint, so follow-up takes a little longer.

Hopefully it was clear we're proceeding with a lot of confidence in this product. We've learned a lot from the data from other studies. We believe that the product has clear differential and differentiation, and obviously our clinical data to date has been encouraging to show its potential to meet the non-inferiority endpoint and potentially more than that is really what we're looking for.

Matthew O'Brien

Got it. Then just real quick for Andrew, can you just maybe frame up the economics to Orchestra pre-the capital raise and now post-the capital raise in terms of what falls to Orchestra from a revenue perspective, now that there's a royalty on top of a royalty, going to Ligand, etc.? Just how does that look? How do we think about how much revenue can accrue to the company quickly and then profitability can accrue to the company quickly once these products get approved? Thanks.

Andrew Taylor

First of all on the revenue front once royalties come online, what you had calculated for revenues from our partners, from Medtronic in particular, is unchanged. So 100% on that line. As it relates to the Virtue product, and maybe I'll have David handle that in a moment, how to sort of think about the future royalty stream coming from the Virtue product, but just to let you know how things are being handled from a Ligand or a Medtronic accounting perspective, basically, as you've seen, at least in these first financials with the Ligand transaction, that it is 100% on the balance sheet as effectively a contingent liability is how it's technically accounted for, and there's some effective interest that accrues there. Over time, the payments that we'll make to Ligand in the future will amortize off of that balance sheet item. So almost none of it is going to hit the P&L, except the sort of non-cash accrual of the interest. So over time, our profitability is almost unchanged from how we would have managed it before. Obviously with some cash differential, but from a P&L perspective, I think we're sort of in a similar boat to the way we were before.

David, do you want to comment a little bit on how folks should think about Virtue in the future in terms of the change from Terumo?

David Hochman

Right, and I just want to add some comments. So just to be clear, the interest implied on Ligand is not built into the instrument; it's part of how these type of structures are accounted for. Obviously, royalty-based revenue interests are fairly commonly used in the biopharma space, novel in terms of us as a med device company.

Also it's worth noting, just to make clear, that the Medtronic convertible note when it converts following approval, once again, we'll book the royalty revenue, and then down further in the P&L we'll credit back to Medtronic 15% of that until we reach the $40 million cap. So we do think that's quite a favorable structure.

With regard to Virtue, as I noted on the call, we think we have now what we're referring to as strategic optionality. Clearly the previous Terumo arrangement I think evidenced one type of unique strategic partnership structure that Orchestra in many ways was founded to pursue; where we shared in the development costs and responsibilities, Virtue, we think, has broad applicability within coronary and peripheral, and some of those indications may require additional trial to get full labeling. We're still evaluating how that's going to happen with competitive products, but certainly as we move from coronary to peripheral, there will be other studies. In our original Terumo arrangement, we had essentially taken responsibility for the trial we're now conducting, Virtue ISR, but Teruma had responsibility for other studies. We also had shared in the responsibilities associated with manufacturing. They were going to be responsible for the device. We're responsible for the drug. We had a royalty arrangement up to 15% and a revenue share arrangement around the drug component.

One opportunity going forward is to—and Terumo is still engaged with their right of first refusal with Terumo or another strategic party to pursue a similar type of partnership, which we think offers P&L costs and other advantages to our partners.

That said, other more typically used structures now are something we could consider, whether that's structured M&A, structured distribution arrangements, or more typical M&A that might include upfront as well as earnout components.

While we're committed to our business strategy and we think it offers huge advantages, we've often had comments from investors and others that this model hasn't yet been proven in the medtech space. And so we see opportunity to continue to pursue what we think is our unique approach, but also to generate value for our shareholders through more typical structures around Virtue. Ultimately, we believe we have a best-in-class asset. We're doing the work to prove it, and we think that asset will have broad strategic interest as we progress in our development and generate more data.

Matthew O'Brien

Thanks so much.

David Hochman

Thanks, Matt.

Operator

Our next question is from Matt Miksic with Barclays. Please proceed.

Matt Miksic

Hey, thanks so much for taking our questions and for the update.

David Hochman

Hey, Matt.

Matt Miksic

Apologies because we're, I don't know if anyone else is juggling a few calls and events this morning, but I know we are, so sorry if we covered this already, David. The SELUTION data presented at TCT and the success with the paclitaxel program, but success of the AGENT launch by Boston should be kind of heartening, I guess, validating of the space. Maybe if there was anything that you took away from, in particular, this (inaudible) data and what do you think it means for the space, or what do you think it tells us or should tell investors about the space, that would be terrific. Then I have one quick follow-up.

David Hochman

Yes, well, I think TCT was another—and this has been a trend for the last few years of TCT and EuroPCR, where the advance of leave-nothing-behind, particularly drug-coated balloons in the coronary continues to march forward steadily. I think it was notable with the late-breaking presentations on the SELUTION data some of the key commentary from the podium and from the panelists. We've known Jeff Moses for a long time, and Jeff, I think the quote was, "Ultimately we're going to have to relearn how to perform PCI or percutaneous coronary intervention with drug-coated balloons." So I think the data continues to drive confidence that drug delivery balloons can be competitive more broadly than just indications like ISR.

With stents, and that continues to, I think, drive a view that while stents have played a very important role in the treatment of coronary artery disease and continue and will likely continue to do so, that if ultimately, first line treatment can be a drug delivery balloon and stents can be used provisionally or let's say in left main artery disease or in proximal lesions, that may be better for patients long-term in terms of avoiding the complications that we now know happen with stents. Whether that's the more rare but devastating consequence of late stent thrombosis or the more common challenge of coronary—or instant restenosis.

There's a steady march there, and I think this idea that physicians and interventional cardiologists are, I think, leaders in the adoption of new innovation, and I think that what we're seeing, what we're hearing from physicians that now are coming on board for our trial, is there's a lot of excitement in using this technology.

At the same time, I think there's still a lot to be learned from the data. In the case of SELUTION, we're awaiting the publications of the data to really look in greater depth in terms of the performance of those studies and garner more information. The data is not yet published, and so there's only so much that we saw, but certainly the idea that a leave-nothing-behind strategy can work in de novo was one of the studies, and that we're now seeing this signal of—and we focus on the single-layer restenosis, kind of mid-teens TLF, which seems to be encouraging but still leave a view from physicians that there's room for improvement.

I think the excitement around the Virtue Trial, the excitement as we're educating more and more physicians on what I detailed is the very deliberate approach we took to building a differentiated device that we think can optimize sirolimus uptake and really bioavailability in the tissue.

I think physicians would like to see technology that gets better results than these trials, and that's why I think we're going to see nice participation in our study, and we're excited about generating that data.

Ultimately, we think this bodes extremely well for Orchestra BioMed, for the Virtue program, and for the commitment we made to taking a novel and differentiated approach to optimize what—and we're carefully choosing our words. These are drug delivery balloons, and I think we really intentionally built what we believe is an optimal drug delivery system to take a drug we know works, we know is safe, we know it's effective as long as you can get enough of it to the lesion, you can keep enough of it available for that healing period of at least 30 days and some say longer, and clearly our drug delivery data—our drug published data shows that we're doing an exceptional job there with Virtue.

We're excited about all the data, and we're excited about what's to come, and our goal is to advance the program steadily, and we're excited to have the capital and the resources to do it.

Matt, you had a follow-up?

Matt Miksic

Yes, yes. On that subject, the feedback we got from TCT, I think everyone probably heard this on the panel, as well the discussion post, the data was small vessel is clearly a place where these devices are going to get some traction, so we took our small vessel numbers up last night, as a matter of fact. (inaudible) out here, small vessel numbers, but still really encouraging. So I'm glad to see you're back on track with Terumo and with the trial.

On BACKBEAT, just congrats on sort of retaining, at least from our view, some optionality around the other potential opportunities for BACKBEAT. The Breakthrough Designation and the potential expansive nature of the scope of those patients, could you—I know you don't want to get ahead of yourself here and trying to get BACKBEAT enrolled in commercial, but could you expand on that a little bit and your thoughts on how wide that could go? Thanks.

David Hochman

Yes, I think, first off, and just to finish up on the Virtue topic, we'll see more and more data coming out of US IDE studies in small vessel de novo, but I think the mindset is that steadily the TAM is going to grow. Once again, the opportunity for Virtue is significant.

I do want to note that ISR looks like probably the best place to differentiate one product from another. The data we showed in single-layer re-stenosis between SELUTION and AGENT and what we're hearing from physicians is it doesn't seem like there's a difference between paclitaxel- and sirolimus-coated balloons in that difficult-to-treat indication. In many disease conditions, kind of the most difficult patients are where you show kind of where one product stands out from another. So we do think ISR is the right place to start. The industry is going to keep moving forward. This trial we think is the ideal trial to showcase Virtue, shifting as you said to BACKBEAT and the broader opportunity to treat high-risk patients that don't yet need a pacemaker indication.

The most important thing that we've noted before is the profile of patients that we have data in at the Breakthrough covers, patients that have uncontrolled hypertension or blood pressure above target, systolic blood pressure above target despite medication, increased cardiovascular risk, preserved ejection fraction, all of these types of comorbid conditions are in the pacemaker population that we've treated and that we're enrolling in the BACKBEAT study. So we're running a big study. It's a double-blind randomized study, and so we think the data will generate not just important to the clinical profile, the regulatory pathway for the pacemaker-indicated population, but we think it's really indicative of the potential value of the therapy beyond.

In terms of our own estimation of that addressable market, which we've put in our public filings and our presentation, we're still looking at a very highly-targeted population. I think we talk about an opportunity of about 3.7 million patients annually worldwide. Within that is roughly a little over a million patients in the U.S. Let's keep in mind that there are 1.2 billion patients worldwide that are believed to have hypertension, upwards of 120 million patients in the United States. So we're still specifically talking about a fraction of 1% of those patients where we think certain key things are true.

One, likely the average age is going to be over 65. That doesn't mean we're excluding, but that's where we see the comorbid conditions where we seem to have the best effect and where we have a therapy that maybe is a standout to benefit patients with hypertensive heart disease, risk of progression to heart failure, and then maybe HFpEF. That's older patients with isolated systolic hypertension, meaning your systolic blood pressure is high but diastolic is normal. This is the most common form of hypertension in older patients. Patients that have diastolic dysfunction, essentially a stiffening of the ventricle that is a key contributing factor to the progression to HFpEF. And then high systolic blood pressure is very common comorbidity amongst HFpEF patients. These are patients that really need a solution that's going to manage the risk of elevated systolic blood pressure, that's going to manage the risk of blood pressure driving workload on the heart that leads to progression to heart failure. So you're trying to avoid heart attacks and strokes, major events, but you're also trying to avoid that steady progression to heart failure.

Once again, the device we're talking about is a device that's implanted in almost every hospital around the world on a regular basis. It's a pacemaker. There are key advances in pacing technology, and Medtronic, our partner has been a key driver that we think are going to enable the future adoption of a therapy like AVIM for a broader patient population.

One of them I talked about briefly on the call, conduction system pacing, where we've learned to optimize ventricular pacing locations where we put the leads to reduce historical risks that I think limited the therapeutic adoption of cardiac pacing therapies.

Leadless technology is another, and I think that the step we took forward with Medtronic's additional investment, at least to state our intent to in the future, incorporate AVIM therapy in a future dual-chamber leadless platform, I think it reflects ours shared view of the potential of the therapies.

Yes, there is still a right of first negotiation with Medtronic. We believe the partnership is really functioning extremely well. We celebrate our partnership with Medtronic. I think they've spoken with their efforts and their dollars in terms of their intention, and we think the next key milestone is the data from the pivotal trial that will I think kind of trigger a discussion on both the business arrangement but also provide a clear point of view on the commercial, clinical, regulatory potential of therapy and what the next steps would be.

The question is, will we really need to do another randomized trial? We're not sure that will be necessary. We'll have to see from the data, but there's a big opportunity and I think we're already well down the path of what needs to happen to validate that opportunity. Then we'll have to figure out—and there's a huge opportunity for the business in figuring out what we do next to reach those patients and align with a partner that very well could be Medtronic.

Matt Miksic

That's great. Appreciate the color. Thank you.

David Hochman

Thanks, Matt.

Operator

Our next question is from Marie Thibault with BTIG. Please proceed.

Marie Thibault

Good morning. Thank you for taking the question.

David Hochman

Hi, Marie.

Marie Thibault

Hi there. I wanted to just have a quick follow-up here on sort of your outlook for operating expense in the coming quarters now that you have two trials underway. Wanted to understand how R&D might change here in the coming quarters. Then also with kind of the change to the Terumo relationship, if there's any updates to the G&A function, any costs that you're having to take on your own. Just a better understanding of how to model that metric.

David Hochman

Andrew, do you want to go ahead?

Andrew Taylor

Yes, I'll take the first part. From a cash burn perspective, just to look back a little bit, on 2025 our average cash burn per quarter was in the sort of $15 million to $16 million range. Might be a small tick up here in the fourth quarter, as you mentioned, bringing on the Virtue Trial now coming online and those associated costs.

I think as we look to 2026, I would anticipate about a 20% increase on the cash burn over the course of the year, so think about sort of higher teens on average, kind of growing to that over the course of the year. Now that we have the acceleration of the two trials, there is some, of course, leverage there with our overhead and G&A and some of executive management, if you will, of the clinical trials, but there's certainly direct costs both on the personnel front and on the patient and hospital costs that will grow over the course of the year.

The one other piece just to keep in mind from an operating expense non-cash but still is impactful for some of your longer term modeling is our non-cash expenses on the stock-based compensation, which we report on is about $3 million a quarter on top of that. Then as we spoke about a little bit earlier, there's some technical accounting that goes into these very standard manifestations of the Ligand deal and the Medtronic deal that are sort of non-cash, not part of the deal, but part of the technical accounting, and that is a non-cash expense of maybe another $1 million to $2 million a quarter. So as you think about the cash expenses sort of growing into the higher teens, I think you layer in a non-cash expense element in the $4 million to $5 million range per quarter and then you get sort of the full picture of the expenses used in the EPS calculation and what have you.

Marie Thibault

Okay.

Andrew Taylor

(Cross-talking)

David Hochman

Yes, and I'll jump in on the second part of the question as to what's the impact of the sort of change in our collaboration structure with Terumo. In the short term and really over the next many quarters, no real change at all. We were always responsible for the execution, financing, operations of the Virtue Trial, the coronary ISR trial. So we've been planning on that for a while and are gearing up to execute that trial as effectively as possible. We also were always responsible for the drug manufacturing, and so that is something that is built into our plans to prepare for scale-up and regulatory approval on the drug side.

We also built, Marie, the device supply chain for the Virtue product. So it's an outsourced supply chain, highly scalable. Ultimately, Terumo was going to assume responsibility for the supply chain as is, so it's a portable supply chain that whether it's Terumo or another partner or potential acquirer, we think any large company could take advantage of that supply chain. There's been a significant trend towards scaled, outsourced supply chains in the interventional field. Some of those components may be good for certain partners to bring in-house over time. So really nothing has changed.

I think from a strategic standpoint, there are opportunities that we, based on the relationship with Terumo didn't have full control of, but now we have the opportunity to think about both what we do from an operational and a development standpoint as well as what we do from a strategic standpoint.

Now we have full control over the coronary program. We're looking closely at what we think we should do next to position Virtue in key next indications like Matt brought up, de novo, small vessel. I would note that Boston Scientific is now running a broad, almost all-comers coronary trial. So we're looking at those. Virtue is not going to be the first product to market. We do think it has the potential to be best. And so like we're doing with the Virtue Trial, I think we're leveraging what we've learned from other studies to really position Virtue to be distinguished with clinical data.

The other thing that I'll note is we now have the peripheral opportunity. While we had a broad partnership with Terumo, we now have the ability to think about potentially different partners for coronary versus peripheral. I think we'll have a lot more to say about both our technical approach and our clinical regulatory approach to the peripheral market, particularly the below-the-knee market over the course of the next year. We're excited to share that. We believe the differentiation of Virtue from a separate drug delivery, liquid drug delivery, that there are device approaches we can take in, let's say the below-the-knee market that are really distinct from what drug-coated balloons do and we're working on that actively, and we'll have more to share with our shareholders and with you as we progress.

So we're excited about it, and we really think we have an exceptional technology that now we are going to drive forward with confidence.

Marie Thibault

Perfect. You actually just answered my second question, which was, would we be seeing any of the sort of pipeline work, the work on peripheral or heart failure or other potential opportunities, so you answered that perfectly. We look forward to it. Thanks so much.

David Hochman

Thanks, Marie.

Operator

Our next question is from Anderson Schock with B. Riley Securities. Please proceed.

Anderson Schock

Hey, good morning. Thank you for the update and taking our questions. On the Ligand royalties, so what are the tiered royalty percentages for the first $100 million and the revenue in excess of $100 million? And is this just for revenue from AVIM and Virtue programs and their current target indications, or will this be for all future revenue across both platforms and any future expansions or additional programs?

David Hochman

Thanks, Anderson, for the question. Andrew, if you don't mind, I'll just jump in.

Andrew Taylor

Absolutely.

David Hochman

The Ligand investment is limited to AVIM therapy and Virtue. The first tier related to our first $100 million of revenue is 17%, essentially fed by both products. Both are in there.

Once we are over $100 million, that royalty rate for Ligand drops to 4%. The 17 drops to 4% and the scope of indications related to Virtue and AVIM is more constrained. So with regard to AVIM, it's only for the treatment of hypertension. Heart failure wouldn't fit into that or other indications. And for Virtue, it's only the coronary market where the royalty or revenue flows would trigger a royalty.

So thoughtful structure. I think the novelty of the structure with Ligand has been a great relationship getting to work with them and we think that there's a big opportunity for them. But as was intentional, we preserve, we think, the significant share of opportunity, particularly if both products are as successful as we intend to make them, we preserve the vast majority of that cash flow opportunity for our shareholders.

Anderson Schock

Okay. Got it. Thank you.

And then could you go over what cases would trigger Terumo's right to first refusal and when it would not? Is this only related to outside parties interested in taking over commercialization of Virtue?

David Hochman

Yes, so it's specific to the coronary market on a global basis and it's with regard to third-party transactions. So in the event—and we're clear about our business model, but there certainly is an opportunity where Orchestra could—we think Virtue is a best-in-class product. It's a huge market. We could take on, in some way, commercialization ourselves. I'm not stating we're intending to do that at all, but that would not trigger this right of first refusal, to be clear.

Third-party transactions—and it could range from a distribution arrangement, some type of strategic collaboration, or a structured or full acquisition of rights or the technology would trigger that right of first refusal, assuming it's for the coronary market. And that right of first refusal, to be clear, is in place only until 90 days after we disclose the Virtue Trial primary endpoint data to Terumo, and that's specific to the disclosure to Terumo. After that 90-day period, the right of first refusal expires. During that ROFR period, if we have a transaction that we want to pursue, we'll notify Terumo, and they'll have 30 days to say, "Yes, we want to exercise our right," and then 90 days to close the transaction on the same terms as what we wanted to pursue with the third party.

We think these are fairly commercial standard terms for this type of right of first refusal. I think it reflects a shared view with Terumo that the coronary opportunity is the larger opportunity on a global basis, and frankly, I think the shared view that the U.S. market is clearly the most compelling opportunity that fits their strategic interest. Obviously we believe Virtue has broader opportunities in peripheral and other indications, and as I just noted, we're excited to share over time more of our thoughts on the pipeline opportunities for Virtue, but this ROFR is specific to coronary.

Anderson Schock

Okay, got it. Thank you for taking our questions.

David Hochman

Thanks, Anderson.

Operator

Our next question is from Josh Jennings with TD Cowen. Please proceed.

Josh Jennings

Hi, good morning. Thanks for taking the question, and congrats on all the progress. I wanted to apologize if this has already been addressed, but a high-level question on AVIM therapy, and just with the increased focus by industry and the clinical community on hypertension and uncontrolled hypertension, with new therapeutics coming on board and the resurgence of renal denervation.

Our recent checks with KOLs suggest that many patients are going to need multiple therapies to get their blood pressure controlled, but maybe just talk about the tailwinds that are in place for AVIM and how you think about AVIM as a complementary therapy alongside new therapeutics potentially and renal denervation.

And then second, just as the pacemaker innovation is moving towards leadless technologies, just help us understand any engineering hurdles in terms of incorporating AVIM into leadless technologies. Thanks for taking the questions.

David Hochman

Yes, thanks, Josh, and great questions. Yes, I think there's—after a lot of years of a limited amount of innovation, hypertension, I think we're realizing some big advances, and it's obviously a huge market, a huge unmet need.

I think drugs and devices are both making progress, and we pay attention to that progress. But we do think that there's a distinct opportunity for AVIM, and that AVIM therapy has a novel opportunity that's quite significant.

You follow closely the progress on renal denervation. Our strategic partner Medtronic has really been the innovation and is poised to be the market leader in renal denervation, which will be the first commercial device-based intervention for hypertension. Recent significant event in terms of national coverage decision and coverage in terms of further evidence development, I think it's a big win for the field, big win for Medtronic.

Notably, we think renal denervation and AVIM therapy are highly complementary to have in the same strategic portfolio. And the national coverage decision, I think, distinguishes one key difference between the target population. The national coverage decision was approved for patients with combined hypertension, meaning elevated systolic and diastolic disease. Not to say that AVIM therapy can't benefit those patients, but as we've noted looking at the MODERATO II data, and as I mentioned today, as patients age the predominant form of hypertension is isolated systolic. In MODERATO II we saw almost 90 percent of the patients had isolated systolic hypertension where you have high systolic blood pressure, but diastolic blood pressure is normal. That condition means that pulse pressure is elevated, which is an independent risk factor for major adverse events – heart attack, stroke, progression to heart failure.

Our data suggests that AVIM therapy really can target systolic blood pressure specifically without requiring or without driving a commensurate reduction in diastolic blood pressure, which is really ideal for those patients. And obviously we've talked about the other benefits in terms of impact on ventricular function and its ability to be incorporated in a very commonly implanted device and be available to patients that need that device for the future. And so we think that really is unique.

As we look at the pharmaceutical developments happening, I think there was new data out from Mineralys and there's an expected approval of the selective aldosterone inhibitors, the ASI field. I think there's new drugs coming for hypertension, but once again, common format—and we've looked at the clinical data—as you see these drugs targeting combined hypertension that they work on both systolic and diastolic blood pressure. The biggest challenge in pharmaceutical therapy for isolated systolic hypertension is finding the right mix of drugs that have an impact on systolic blood pressure but don't have too much of an impact on diastolic blood pressure. That's been a real challenge for the treatment of hypertension in older, higher risk patients, and that's where we think AVIM could really be an attractive therapy as we progress forward.

Then your last question, notably, this is atrial ventricular interval modulation. It's important for at least the therapy as we're currently delivering it in the BACKBEAT trial and in what we've done to date to be able to sense-pace both the atria and the ventricles, so we're talking about dual-chamber devices.

The predominant form of leadless technology for the last number of years has been single chamber leadless technology. That's changing. I think there's opportunity for probably significant device differentiation between the companies in the approach to dual-chamber and leadless. I think that as we see that unfold, ultimately we believe that move is going to be a big opportunity for the broader potential adoption of AVIM therapy as we see kind of next generation leadless technology emerge.

It will, in our opinion, still take a long time to transition the global market from transvenous pacemakers to leadless, both from a cost and technology availability standpoint. So dual-chamber transvenous pacemakers are going to be here for a long time. They're getting better. They are driving conduction system pacing, which is also highly complementary to our therapy. So we think AVIM therapy is very well positioned in terms of taking advantage of the core advances in cardiac pacing therapy as well as carving out an important landscape for the treatment of high risk isolated systolic hypertension in older comorbid patients.

Josh Jennings

Appreciate those thoughts.

David Hochman

Thanks so much, Josh.

Operator

Our next question is from Yi Chen with H.C. Wainwright. Please proceed.

Eduardo

Hi, this is Eduardo on for Yi. Thanks for highlighting the achievements of the year.

Just following up on this AVIM and the dual-chamber versus single chamber, could you explain a little bit more about switching behaviors in that population? Obviously you need atrial and ventricular stimuli for the AVIM therapy to work, and now that you have this expanded eligibility for the people having the Azure and Astra, what was the reasoning for, I guess, excluding them initially and now bringing them into the fold? What's their kind of predisposition towards receiving the AVIM complementary therapy?

David Hochman

Sure. I think I understand the question. First off, dual-chamber pacemakers are the dominant type of device that are implanted in patients. Upwards of 85% to 90% of devices are dual-chamber devices. It's typically patients with high, for example, atrial fibrillation burdens where you might put single chamber devices. So we're not—we're taking advantage of that as the most common form of pacing. The current therapy requires and does active atrial and ventricular pacing or modulation of AV. That's not to say that as we develop the therapy, we haven't thought of other strategies, but that really is the first iteration of what we're doing today.

I think the question related to the trial was sort of the approach we took to broaden the eligibility. Really, I think one of the challenges we faced with Medtronic as our partner still was AVIM therapy represents a new capability targeting a new condition that previously pacing therapies didn't offer. So we have the challenge of—in terms of implementing a pivotal clinical trial of finding an optimal way to make that therapy available. We took advantage of the fact that our partner is the global market leader and made this available as a download for the clinical trial to their most commonly implanted devices, Azure and Astra. However, initially, we were restricted to only patients that recently received a device and had a very narrow window in which to do all the screening required to enroll patients.

That was a real challenge in 2024 with the trial and we quickly adapted in terms of regulatory process to make protocol changes. Nothing really happens quickly in clinical trials. It's all done very thoughtfully and carefully. So we recognized the challenge, adapted the protocol, but it's taken time to implement that and then learn how to optimize.

So we implemented a change in 2024 that allowed us to look at patients that had been implanted with those devices going back a year and screen those and also to create flexibility in terms of what we call the look-forward patients, patients that have been recently implanted.

As soon as we saw that benefiting screening enrollment, frankly, we recognized why did we limit it to a year? We also identified some other just procedural steps that were just challenging for the workflow at sites, and that's what the next protocol amendment that we've almost now fully implemented did. Now we can look back to patients that—practically we're looking at about seven years. We want to make sure the patients have enough battery life on their device to finish the follow-up of the study.

I think we've streamlined the approach to look-forward. And both approaches are working. And we have sites in the U.S. and Europe that have significant look-back populations, and they're beginning to figure out how to engage those patients. Then we have sites that are being quite successful in the trial that are predominantly doing what we call the look-forward new implant approach.

What we like about this is we really think the BACKBEAT study will ultimately look like a real-world study in terms of the practical utilization and impact of AVIM therapy where we're going to have patients that are new to their pacemaker that have AVIM therapy activated, and then patients where we're activating the therapy even though they've been (inaudible) for years. We also added replacement devices, which were in the MODERATO studies, but just sort of in terms of being highly conservative, initially were not allowed in the BACKBEAT study. Now they are. About 25%, roughly, of pacemaker implant volume is box changes, or essentially the pacer device is swapped out for a new device. That happens roughly at 10- to 12-year intervals. So now we're seeing those patients in the trial as well.

I really like the way the protocol is set up. Unfortunately we lost time and enrollment learning these lessons, but that is both the burden and the opportunity of being an innovator, bringing a new capability to an existing market, and having to thoughtfully design what we think can be a very powerful clinical study that hopefully can drive this as a standard of care, certainly for the pacing population, and hopefully beyond.

Hopefully that was what you were looking for in terms of your question.

Eduardo

Yes, that's really helpful. If I could ask also on the clinical data supporting the Virtue Trials, you mentioned improving TLR relative to competitors. I'm curious what AGENT's rates of heart failure and major cardiovascular event outcomes are in that three-year period. If you would expect—how does the Virtue compare in regard to that, or if it's still kind of early on in the lifecycle…?

David Hochman

I think heart failure is—obviously development of heart failure may be unrelated to coronary artery disease specifically in the patient, but what we're looking at in TLF is a combination of two things. One, major adverse cardiac events in the patient, and then the second one you noted is TLRs are target lesion revascularization. Essentially, did you need to go and retreat that same lesion?

I think what the clinical community has noted about the AGENT data is, now that two-year data was made available earlier this year, the goal of a leave-nothing-behind strategy is to avoid acute devastating events as well as restenosis. So what you're hoping for is you get a good outcome in the first year. That's that first year target lesion failure. But then you'd like to—by not having an additional stent in there, additional metals, see kind of low event rates going forward.

In the AGENT study, the two-year data showed that target lesion failure increased by I think around 53% from one year to two years. So there was a significant number of additional events, both TLRs and MACE events in those patients.

Obviously, in the SABRE study, the Virtue, it's a smaller study, frankly done before I think technique. One of the things we're doing, we're learning, and I talked about how physicians are relearning PCI. Well, using drug delivery balloons involves imaging, vessel preparation, use of technologies like atherectomy and IVL, and just really making sure you kind of optimize prior to delivering the drug delivery balloon, delivering the drug, the preparation of the lesion. Frankly, the SABRE study didn't really happen when all of that technique was optimized.

Nonetheless, we saw in single-layer restenosis a very low 2.8% one-year TLF. And then really what we were super excited about is that there were no TLRs in those patients from one year to three years. So to me, will we be able to repeat that? You know, that's an exceptional result. Frankly, we don't have to repeat that to be able to still distinguish Virtue. But that gives us a lot of hope that Virtue is delivering the promise of leave-nothing-behind. Great one-year results and hopefully a durable result that doesn't require patients to get retreated.

We're excited now about scaling up and seeing in now an environment where physicians are really optimizing their clinical practice and using these products on a regular basis. Our product performs in that environment relative to the current market leader AGENT. And Boston Scientific has done a great job with the studies, with the reimbursement, and clearly is having great success in the market. They're one of the best companies out there to open up and change clinical practice. So we've been rooting for them, and we're looking forward to our data.

Eduardo

Great. Thanks so much for taking the questions.

Operator

With no further questions, I would like to turn the conference back over to David for closing remarks.

David Hochman

We really appreciate everyone's time and attention to our update. We really thank everyone for the questions, very thoughtful. We are going to continue to focus on execution, having the resources we have. We look forward to sharing more information and updates with our shareholders and with the Street as we progress. Thank you for your time today. Have a great day.

Operator

Thank you. This will conclude today's conference. You may disconnect at this time, and thank you for your participation.

Exhibit 99.2


Orchestra
BioMed
Business Update
November 2025
Nasdaq: OBIO

Forward-Looking Statements

This presentation has been prepared for informational purposes only from information supplied by Orchestra BioMed Holdings, Inc., referred to herein as "we," "our," "Orchestra BioMed," and "the Company," and from third-party sources indicated herein. Such third-party information has not been independently verified. Orchestra BioMed makes no representation or warranty, expressed or implied, as to the accuracy or completeness of such information.

Certain statements included in this document that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements relating to the potential safety and efficacy of our product candidates, the initiation, enrollment and timing of our planned pivotal trials and reporting of top-line results, expected market sizes for our product candidates, the ability of our partnerships to accelerate clinical development and the benefits of Breakthrough Device Designation. These statements are based on various assumptions, whether or not identified in this document, and on the current expectations of the Company's management and are not predictions of actual performance. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as and must not be relied on as a guarantee, an assurance, a prediction, or a definitive statement of fact or pr and circumstances are difficult or impossible to predict assumptions. Many actual events and circumstances are bey Company. These forward-looking statements are subject to uncertainties, including changes in domestic and foreign busi political, and legal conditions; risks related to regulatory app product candidates; the timing of, and the Company's abilit regulatory and business milestones; the impact of competitiv candidates; and the risk factors discussed under the heading "I the Company's annual report on Form 10-K filed with the U.S. Commission on March 31, 2025 as updated by any risk facto heading "Item 1A. Risk Factors" in Part II of the Company's subs reports on Form 10-Q.

The Company operates in a very competitive and rapidly chan risks emerge from time to time. Given these risks and unce cautions against placing undue reliance on these forward-loo only speak as of the date of this presentation. The Compa undertakes no obligation to update any of the forward-loo herein, except as required by law.

Key Investment Highlights

Leveraging Partnerships to Bring Innovation to Patients & Yield Exceptional Futu

Pivotal Stage, High-Impact Therapies

AVIM Therapy
Programmable, pacemaker-delivered treatment for high blood pressure and hypertensive heart disease

Virtue SA
Proprietary, non-coated angioplasty system for ath disease and other

Large, Established Target Markets

Hypertensive Heart Disease:
>$17B annual global opportunity

Atherosclerotic Arte
>$10B annual global

Partnership-Enabled Business Model

Strategic collaboration
Medtronic
Double-digit revenue share

Strategic rights a
TERUM
Right of First Refusal in c

Funded Through Key Milestones

$147M+ in new capital raised since August 2025, led by strategic inv

$31.6 million committed by Medtronic

$40 million committed by LIGAND

$30 millio
TE

Expected cash runway through key milestones into Q4 2027 inclu

BACKBEAT Study enrollment completion & primary results readout

Virtue Trial enrollme

Over $147M in Strategic-Driven Financing Secured Since Aug

$85M of Strategic Capital Commitments + $62.6M Equity Financing → Expected to Provide Runv

Medtronic

- **Global market leader in cardiac pacing therapy** and existing collaborator for AVIM Therapy program
- **$31.6 million** additional strategic investment commitment brings total investment amount to **$81.6 million**
- **Collaboration expansion** provides potential development pathway for future AVIM-enabled leadless pacemaker integration

LIGAND

- **Established biopharma investor** with tie in Orchestra's future AVIM Therapy and V revenues
- **$35 million** committed to purchase royal interest; plus **$5 million** equity investme
- Ligand's long-term capital commitment i commercial success and **reflects Orchest future royalty-based revenue opportuni**

TERUMO

$30 million total payments associated with new strategic rights agreements

Terumo ROFR Agreement Highlights Strategic Interest & C

- Orchestra **developed Virtue SAB from concept stage, owns all related IP, conducted all prior studi retains all development and distribution rights** in all indications
- Terumo is a global leader in interventional cardiology devices: **>$2.4B in annual revenues**[1]
- Terumo purchased **ROFR** for **Virtue SAB** transactions with respect to the **global coronary market**
  - Orchestra free to engage actively with all strategic parties and solicit proposals
  - Terumo has 30 days following notice of a third-party proposal acceptable to Orchestra to exercise ROFR
  - Expires 90 days after disclosure of primary endpoint data from the Virtue Trial
- **$65M in total payments and investments** received over time **from Terumo**
  - $10M paid in consideration of ROFR, plus $20M purchase of non-voting preferred with minimum $12/share after Virtue Trial results announced
  - Initially paid $30M for Virtue SAB rights under original distribution agreement plus $5M equity investment

ROFR = Right of First Refusal; [1]Based on Terumo's consolidated financial results for the fiscal year ended March 31, 2025.

Virtue® SAB Overview

Recently Launched U.S. IDE Pivotal Study and Robust Reimbursement Landscape

- Orchestra BioMed is sponsoring and in full operational control of **Virtue US coronary IDE trial** randomizing 1:1 to Boston Scientific's AGENT PCB
- **Expected enhanced reimbursement** supporting large commercial opportunity

Virtue SAB is Designed to Redefine Arterial Drug Delivery with Significant Differentiation

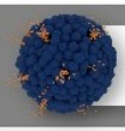
- **Proprietary SirolimusEFR™ extends release** of therapeutic levels of "gold-standard" drug through **critical healing pe**
- **Non-coated** microporous balloon designed to **protect drug in transit to consistently deliver large liquid dose** overcoming the limitations of drug-coated balloons
- **Best-in-class clinical data from SABRE pilot study** shows promising and durable safety and efficacy in coronary ISR, with 2.8% TLF at 1 year and 0% TLR between 1-3 years[1,2,3]

Paradigm Shift Unlocks High-Growth Opportunity in Large $10B Established Market[4]

- **Drug-coated balloons (DCB) emerging as new standard of care** for key coronary and peripheral indications
- Boston Scientific's AGENT Paclitaxel-coated balloon US commercialization underway with **positive indications of sales growth**

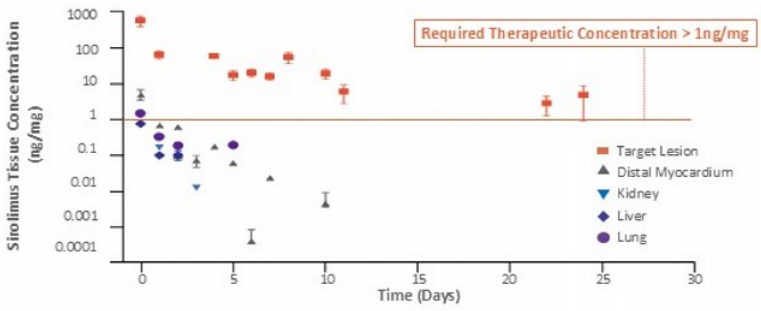
[1]Verheye et al. JACC Cardiovasc Interv 2017 Oct 23;10(20):2029-2037. DOI: 10.1016/j.jcin.2017.06.021. [2]Revised per protocol analysis set meets the criteria of the proposed In-Stent Restenosis IDE study population. [3]Granada 3-Year Clinical Results TCT 2018. 4Total addressable market in 2025 based on company estimates.

Virtue® SAB – Optimal Drug, Dose and Delivery



SirolimusEFR™ | Protected Delivery of Extended Release Sirolimus | Microporous AngioInfusio

Published Data Demonstrates Therapeutic Tissue Concentrations Through Critical Healing Period (~30 Days)[1]

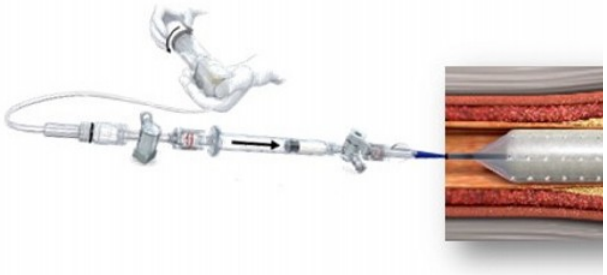


N = 753
porcine coronary artery segments

[2]Lung, liver & kidney below level of assay quantification (0.1 ng/mg) in <1 week

Large Liquid Dose Loaded and Protected i Delivered Through the Micropores Durin

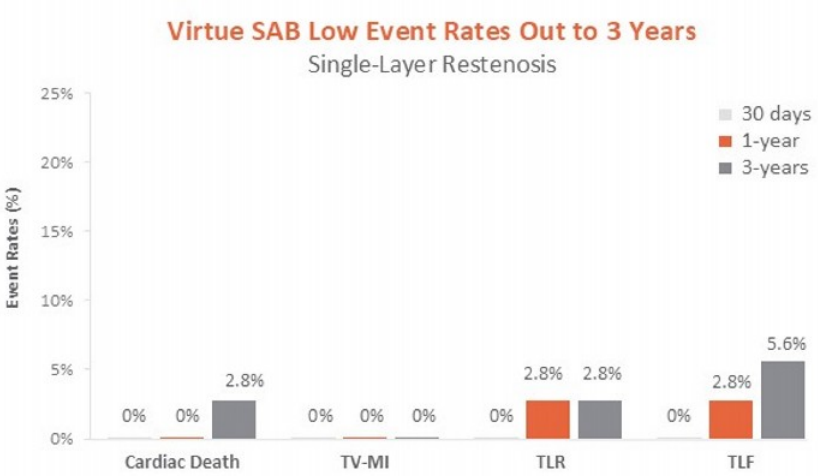
NO coating = NO drug loss in transit, NO rush and NC



[1]Granada et al. EuroIntervention 2016;12:740-747. [2] Animals included in the analysis of distant organs received average dose of 20.4 mg ≈10X the largest clinical dose

Compelling SABRE Trial Results in Coronary ISR Patients

Virtue® SAB demonstrated encouraging safety and efficacy results in patients with coronary in-stent restenosis (ISR) in prospective, multi-center SABRE Trial[1,2,3]



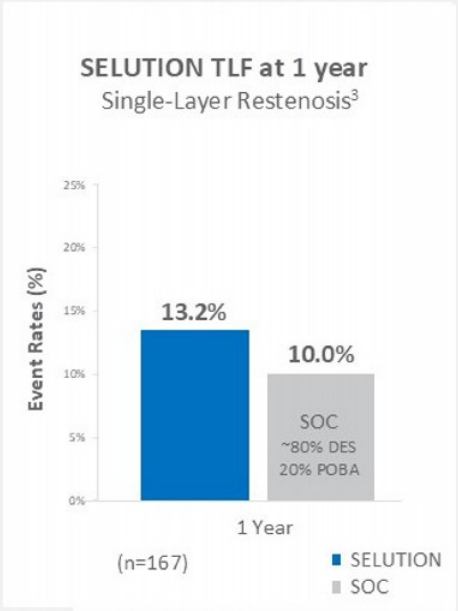
Low 2.8% Targe
(TLF) at 1 year

0% Target Lesio
(TLR) between

Low 0.12mm La
(LLL) at 6-month

[1]Verheye et al. JACC Cardiovasc Interv 2017 Oct 23;10(20):2029-2037. DOI: 10.1016/j.jcin.2017.06.021. [2] Revised per protocol analysis set meets the criteria of the proposed In-Stent Restenosis IDE study population. [3]Granada 3-Year Clinical Results TCT 2018.
Definitions: Target lesion failure (TLF), late lumen loss (LLL), target lesion revascularization (TLR) and Myocardial Infarction (MI).

AGENT & SELUTION4ISR IDE Trial Results Show Clear Opportunity for Virtue SAB



Target Lesion
13.5% (AGEN
(SELUTION)
(TLF) at 1 yea

AGENT 53%
increase in T
from 1 to 2 y

No angiograp
in both IDE
AGENT LLL =
months[4]; SEL
reported for

Adapted from 2 separate IDE Trials

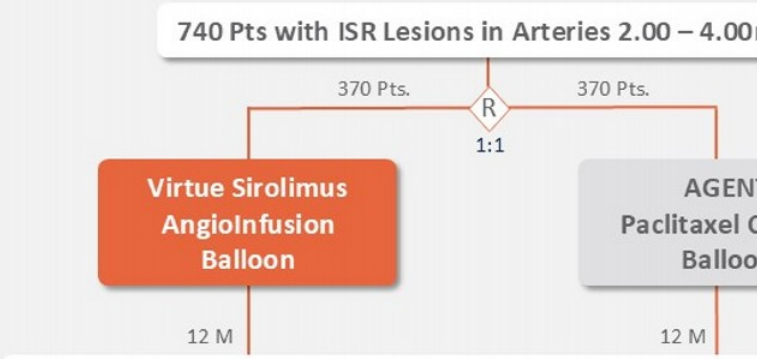
[1]Yeh RW, Shlofmitz R, Moses J, et al. JAMA. 2024;331(12):1015–1024. doi:10.1001/jama.2024.136. [2]Moses, J Two-Year Outcomes from the AGENT IDE Trial CRT 2025. [3]Cutlip et al. SELUTION4ISR Clinical Trial TCT 2025. [4]Boston Scientific AGENT DCB Brochure 2017. ***Definitions:*** Plain old balloon angioplasty (POBA), Standard of care (SOC), late lumen loss (LLL)

The Virtue Trial – U.S. Randomized Pivotal Coronary ISR T

Designed to Secure Regulatory Approval & Showcase Differentiation of Virtue SA

Virtue Trial

- FDA IDE approved
- 1:1 RCT vs AGENT
- N=740
- Up to 75 US Sites
- Primary endpoint 12-Month TLF
- Planned initiation 2H 2025



Primary Endpoint: Target Lesion Failure (TLF) at 12 months

- Primary analysis non-inferiority comparison
- Additional superiority test performed upon confirming no

AVIM Therapy Overview

A Purpose-Built Solution for HTN Patients with Increased Risk in $17B Market

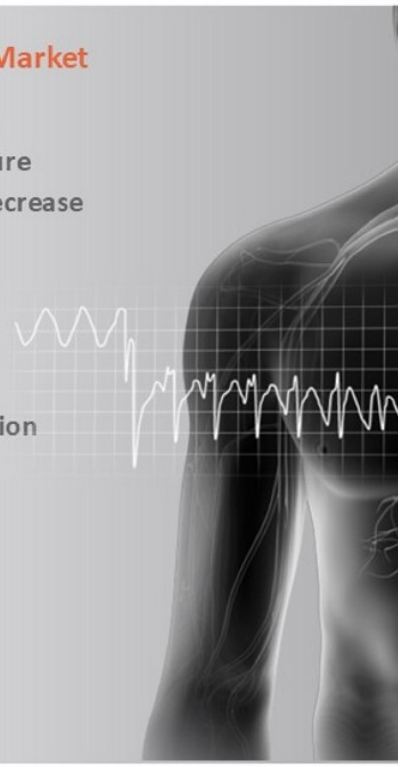
- Hypertension is the **leading global risk factor for death, affecting 1.2B patients**
- Uncontrolled HTN in older, higher-risk patients **drives MI, stroke and heart failure**
- Reductions as small as 5 mmHg in office systolic blood pressure **substantially decrease the relative risk of major cardiovascular events and conditions**

Novel, Programmable, Always-On Therapy

- Patented therapy delivered as **firmware enhancement to pacemaker**
- Designed to drive **immediate, substantial and sustained blood pressure reduction**
- Robust body of clinical and mechanistic data

FDA Breakthrough Designation for Beachhead Market and Beyond

- Initial target is pacemaker population, where **HTN is the #1 comorbidity**
- Potential to expand to **millions of HTN patients with increased CV risk**
- Potential benefit in **HFpEF prevention and treatment**



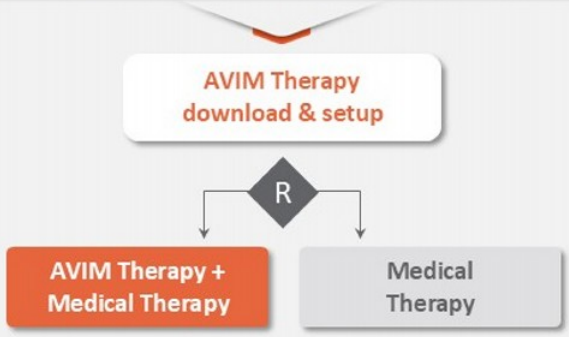
The BACKBEAT Study – Global Pivotal Hypertension Trial

Designed to Secure Regulatory Approval & Showcase Novel Approach to Blood Pressure M

BACKBEAT
GLOBAL PIVOTAL STUDY

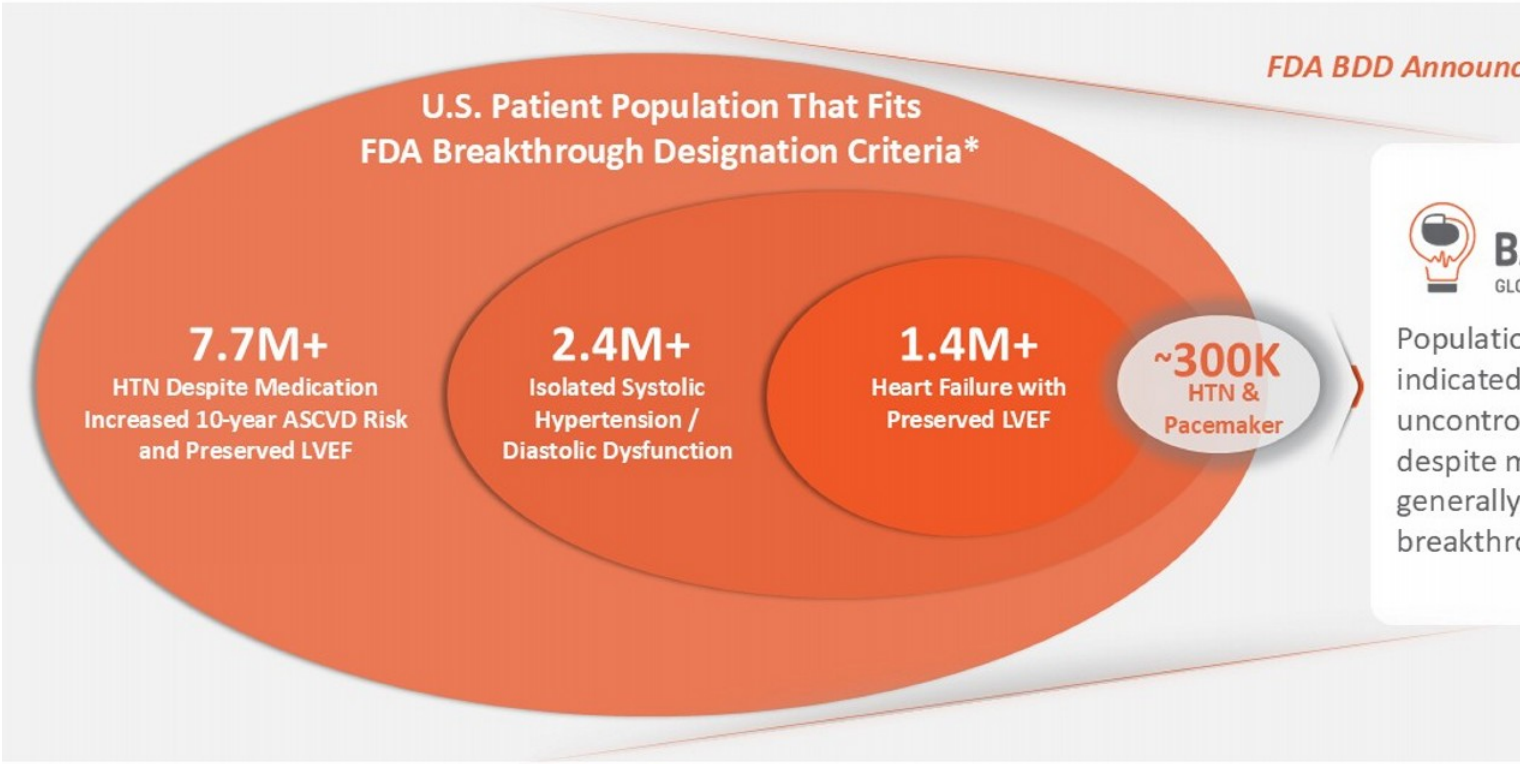
- Randomized, prospective, multi-center, double-blind, controlled trial
- N=500; 130+ sites in U.S. and EU
- Estimated completion of enrollment mid-2026

Patients previously implanted with or indicated for a **Medtronic Astra™ o**
dual-chamber pacemaker who have hypertension despite 1-3 anti-HTN me



- **Primary Efficacy Endpoint:** Mean change in 24-hour aSBP at 3-months
- **Primary Safety Endpoint:** Freedom from unanticipated serious adverse device ev
- **Additional Secondary Endpoints:** Efficacy and safety endpoints after 12-month f
- Option to crossover to open-label **+24 months unblinded follow-up phase**

FDA Breakthrough Device Designation Highlights Potential For AVIM Therapy to Impact Hypertensive Heart Disease



*Based on company estimates.

Favorable Impact on Hypertensive Heart Disease

AVIM Therapy Clinical Results Show Potential to Treat ISH, Induce Reverse Remodeling, and Improve Dias

Significant Reduction in Challenging-To-Treat Isolated Systolic Hypertension (ISH)[1]

>88% of AVIM Therapy patients in MODERATO II had ISH

– 9.5 mmHg
in 24-Hour aSBP
at 6 months

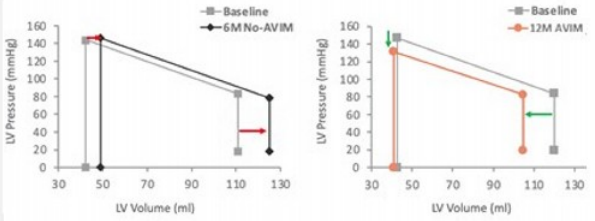
– 15.8 mmHg
in oSBP
at 2 years

– 9.6 mmHg
Δ in Ambulatory PP
at 6 months

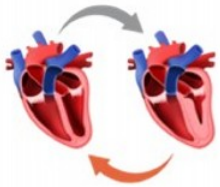
– 13.9 mmHg
Δ in Office PP
at 2 years

Increased Pulse Pressure (PP) an independent risk factor for heart failure & stroke[2]

JACC EP: AVIM Therapy Induced Reverse Remodeling in Noninvasive PV Loop Study[1,3]



Control Group Developed Ventricular Remodeling



AVIM Therapy Induced Reverse Remodeling

JACC Advances: Im Dysfunction (DD) In Analy

>61% of AV MOD

- AVIM therapy **signifi** patients with and wi
- AVIM therapy **impro relaxation and impr compliance** (significa E/A)

Retrospective, treatment-blinded ana from MODERATO II, hypertensive pac and NYHA class < II, with indepe

[1]Burkhoff MODERATO II Study 2-Year Results TCT 2021. [2]Vaccarino V, et al. Am J Cardiol. 2001 [3]N=14 AVIM therapy and n=11 control group. [4]Fudim M, THT'25. ***Definitions***: aSBP (ambulatory Systolic Blood Pressure), oSBP (Office Systolic Blood Pressure), LV (Left Ventricular), PV (Pressure Volume), M (Months). LVEF (Left Ventricular Ejection Fraction), NYHA (New York Heart Association), SBP (Systolic Blood Pressure).

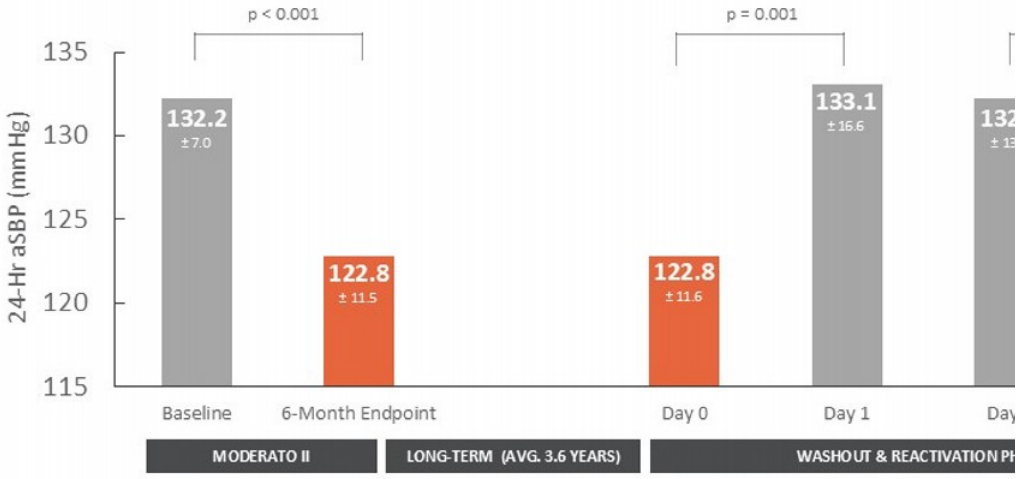
AVIM Therapy Demonstrates Sustained aSBP Reductions w Reproducible Effect and No Rebound Hypertension

16 MODERATO II patients with long-term follow-up & no increase in average number of meds had AVIM therapy de-activated & re-activated

Immediate, substantial, and sustained reduction in aSBP seen across all study phases[1]

Potential to halt hypertensive heart disease progression: aSBP returned to historical baseline after an average of 3.6 years[1]

No rebound HTN observed during washout phase[1]



[1]Kalarus et al., Time Course of Changes in Blood Pressure Upon Cessation of Chronic Atrioventricular Interval Modulation (AVIM) Therapy, HRX 2025 abstract. ***Definition:*** aSBP (Ambulatory Systolic Blood Pressure), HTN (Hypertension), AVG (Average).

Key Investment Highlights

Leveraging Partnerships to Bring Innovation to Patients & Yield Exceptional Futu

Pivotal Stage, High-Impact Therapies

Large, Established Target Markets

Partnership-Enabled Business Model

Expected Funding into Q4 2027

Bringing Medical Innovations to Life Through Partnerships