UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2025

OR

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

For the transition period from _____ to _____

Commission file number: 001-39421

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

Delaware	**92-2038755**
(State or other jurisdiction of incorporation or organization)	**(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

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 Stock Market LLC

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates as of June 30, 2025 the last business day of the registrant's most recently completed second fiscal quarter was approximately $63.4 million as computed by reference to the closing price of the common stock on the Nasdaq Global Market on that date.

As of March 10, 2026, the registrant had 58,520,901 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this report incorporates information by reference from the Company's definitive proxy statement, which proxy statement is due to be filed with the Securities and Exchange Commission not later than 120 days after December 31, 2025.

Table of Contents

Unless the context indicates otherwise, references in this Annual Report on Form 10-K to the "Company," "Orchestra," "we," "us," "our" and similar terms refer to Orchestra BioMed Holdings, Inc., a Delaware corporation formerly known as Health Sciences Acquisitions Corporation 2, and its consolidated subsidiaries.

Certain information contained in this Annual Report on Form 10-K relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this Annual Report on Form 10-K, we have not independently verified the market and industry data contained in this Annual Report on Form 10-K or the underlying assumptions relied on therein. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source. Notwithstanding the foregoing, we are liable for the information provided in this Annual Report on Form 10-K. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those referred to in "Part I, Item 1A. Risk Factors" in this Annual Report on Form 10-K. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this report, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of clinical trials, research and development costs, regulatory approvals, timing, and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important factors that are in some cases beyond our control and may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

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

- our ability to raise financing in the future, including our ability to borrow additional funds under our current debt financing arrangements;
- our receipt of committed capital, including the payment of the Second Installment under the Royalty Purchase Agreement (each as defined herein) and the timing of the funding of the Medtronic Loan Agreement (as defined herein);
- our success in retaining or recruiting, or changes required in, our officers, key employees or directors;
- our ability and/or the ability of third-party vendors and partners to manufacture our product candidates;
- our ability to source critical components or materials for the manufacture of our product candidates;
- our ability to achieve and sustain profitability;
- our ability to achieve our projected development and commercialization goals;
- the rate of progress, costs and results of our clinical studies and research and development activities, including, among other things, the date by which we expect to complete enrollment of our BACKBEAT global pivotal study;
- market acceptance of our product candidates, if approved;
- our ability to compete successfully with larger companies in a highly competitive industry;
- changes in our operating results, which make future operations results difficult to predict;
- serious adverse events, undesirable side effects that could halt the clinical development, regulatory approval or certification, of our product candidates;
- our ability to manage growth or control costs related to growth;
- economic conditions that may adversely affect our business, financial condition and stock price;
- our reliance on third parties to drive successful marketing and sale of our initial product candidates, if approved;

- our reliance on third parties to manufacture and provide important materials and components for our products and product candidates;
- our and our partners' abilities to obtain necessary regulatory approvals and certifications for our product candidates in an uncomplicated and inexpensive manner;
- our ability to maintain compliance with regulatory and post-marketing requirements;
- adverse medical events, failure or malfunctions in connection with our product candidates and possible subjection to regulatory sanctions;
- healthcare costs containment pressures and legislative or administrative reforms which affect coverage and reimbursement practices of third-party payors;
- our ability to protect or enforce our intellectual property, unpatented trade secrets, know-how and other proprietary technology;
- our ability to obtain necessary intellectual property rights from third parties;
- our ability to protect our trademarks, trade names and build our name recognition;
- our ability to maintain the listing of our common stock on The Nasdaq Stock Market LLC ("Nasdaq");
- the success of our licensing agreements; and
- our public securities' liquidity and trading.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations, and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this report and are subject to a number of risks, uncertainties, and assumptions described under the headings "Item 1A. Risk Factors" in Part I of this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We do not plan to publicly update or revise any forward-looking statements contained herein whether as a result of any new information, future events, or otherwise, except as required by law.

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

SUMMARY OF RISK FACTORS

The following is a summary of some of the risks and uncertainties that could materially adversely affect our business, financial condition and results of operations. This summary should be read together with the more detailed description of each risk factor disclosed under "Item 1A Risk Factors" contained in Part I of this Annual Report on Form 10-K.

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

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

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

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

- Even if we obtain all necessary U.S. Food and Drug Administration ("FDA") approvals, our product candidates may not achieve or maintain market acceptance and may be subject to additional regulatory requirements post-approval.

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

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

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

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

- We, in conjunction with our partners, intend to expand sales of our products internationally in the future, but we and our partners may experience difficulties in obtaining regulatory approval or certification or in successfully marketing and distributing our products internationally even if approved or certified.

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

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

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

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

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

- Our medical device products, if approved or certified, may cause or contribute to adverse medical events or be subject to failures or malfunctions that we are required to report to the FDA or similar foreign regulatory authorities, and if we fail to do so, we would be subject to sanctions that could harm our reputation, business, financial condition and results of operations.

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

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

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

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

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

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

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

- The future sales, or the perception of future sales, of shares by existing stockholders and future exercise of registration rights may adversely affect the market price of our common stock.

PART I

Item 1. Business

Our Vision

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

Our Company

We are a biomedical innovation company accelerating high-impact technologies to patients through strategic collaborations with market-leading global medical device companies. We are led by a highly accomplished, multidisciplinary management team and a board of directors with extensive experience in all phases of therapeutic device development. Our business was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by our founding team.

Our flagship product candidates are Atrioventricular Interval Modulation Therapy ("AVIM Therapy") for the treatment of hypertension ("HTN"), the leading risk factor for death worldwide, and Virtue® Sirolimus AngioInfusion™ Balloon ("Virtue SAB") for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. We have an exclusive license and collaboration agreement with Medtronic, Inc. (an affiliate of Medtronic plc) ("Medtronic") for the development and commercialization of AVIM Therapy for the treatment of uncontrolled HTN in patients indicated for a cardiac pacemaker (as amended, the "Medtronic Agreement"). We are actively conducting a double-blind, randomized, global pivotal study (the "BACKBEAT study"), enrolling up to 500 patients with uncontrolled hypertension who are indicated for a Medtronic dual-chamber pacemaker, with enrollment completion currently planned for mid-2026. We recently initiated patient enrollments in the Virtue SAB in the Treatment of Coronary In-Stent Restenosis ("ISR") Trial (the "Virtue Trial") for our U.S. investigational device exemption ("IDE") pivotal study randomizing Virtue SAB vs. Boston Scientific Corporation's AGENT™ drug-coated balloon. Designed to support regulatory approval of Virtue SAB, the Virtue Trial is expected to enroll 740 patients in the United States with enrollment completion currently planned for mid-2027.

Our Flagship Candidates

AVIM Therapy

AVIM Therapy is a bioelectronic therapy candidate designed to immediately, substantially and sustainably lower blood pressure. AVIM Therapy can be fully integrated as a firmware upgrade to standard cardiac pacemakers. HTN is the most common comorbidity in the pacemaker population affecting over 70% of the pacemaker-indicated patients, making AVIM Therapy a potentially highly attractive therapeutic solution for these patients. AVIM Therapy may offer therapeutic benefits to HTN patients not yet indicated for a pacemaker who have uncontrolled systolic blood pressure despite medical therapy and have high cardiovascular risk factors, such as Isolated System Hypertension ("ISH"), Diastolic Dysfunction ("DD") and additional serious medical comorbidities including hypertensive patients with heart failure with preserved ejection fraction ("HFpEF").

Although the safety and efficacy profile has not yet been established by any regulatory body, AVIM Therapy previously showed encouraging results in clinical studies conducted by Orchestra BioMed with its Moderato™ device, including the MODERATO II study, a prospective, multi-center, randomized, double-blind pilot study (the "MODERATO II study)" and in the MODERATO I study, a prospective, multi-center, single-arm open label study of patients with uncontrolled HTN and an indication for a pacemaker. We have also published additional clinical study results demonstrating favorable mechanistic and cardiac function effects of AVIM Therapy on patients with blood pressure above target thresholds.

On June 30, 2022, we entered into an exclusive license and collaboration agreement with Medtronic, one of the largest medical device companies in the world, for the development of AVIM Therapy for the treatment of HTN in pacemaker-indicated patients (the "Medtronic Collaboration"). The Medtronic Collaboration provides us with development, clinical and regulatory support for the BACKBEAT (**B**radyc**A**rdia pa**C**ema**K**er with AVIM for **B**lood pr**E**ssure tre**A**tmen**T**) global pivotal study ("BACKBEAT study"). Upon regulatory approval, if received, Medtronic will have the exclusive global rights to commercialize AVIM Therapy for this target population. If AVIM Therapy is approved and successfully commercialized, we will share meaningfully in the revenues generated from Medtronic's sale of AVIM-enabled pacing systems. Medtronic has a right of first negotiation with respect to AVIM Therapy for the treatment of HTN in non-pacemaker patients.

On August 5, 2025, we announced that we and Medtronic had amended the Medtronic Collaboration to provide a pathway for potential integration of AVIM Therapy into future Medtronic leadless pacemakers. At the same time, we announced that Medtronic made an additional equity investment in the Company of $11.6 million and committed $20 million in exchange for a secured subordinated promissory note convertible to a capped revenue share credit. During 2022, Medtronic invested $40.0 million in the Series D Financing and entered into a $10.0 million forward purchase agreement in support of the Business Combination (as defined below).

We estimate that the total addressable market for pacemaker-indicated patients with HTN comprises more than 1,000,000 patients worldwide per year and represents a potential annual revenue opportunity for us and Medtronic of over $2.4 billion. We further estimate that the annual market for highly selected patients with uncontrolled hypertension that are not yet indicated for a pacemaker but have high cardiovascular risk and key co-morbidities, including HFpEF, comprises at least 3.7 million patients worldwide, or approximately 0.3% of the global HTN population, and represents a potential annual revenue opportunity for Orchestra BioMed and a strategic partner of over $15 billion.

On April 22, 2025, we announced that the FDA had granted Breakthrough Device Designation ("BDD") for an implantable system for delivery of AVIM Therapy using conduction system pacing to reduce blood pressure in patients with preserved left ventricular systolic function and uncontrolled hypertension with increased high ten-year atherosclerotic cardiovascular disease ("ASCVD") risk, despite the use of anti-hypertensive medications or in patients who may have intolerance to anti-hypertensive medications. Orchestra BioMed estimates that there are over 7.7 million patients in the U.S. that meet the criteria for the BDD for AVIM Therapy.

On September 19, 2023, we announced that the FDA granted us investigational device exemption ("IDE") approval to initiate the BACKBEAT study to treat HTN in patients indicated for a pacemaker. The study is a double-blind, randomized study that is expected to enroll up to 500 patients that have previously been implanted with a Medtronic dual-chamber pacemaker (Azure® or Astra®) and have blood pressure above target despite medical therapy at up to 130 clinical sites worldwide. Patients will be randomized 1:1 to AVIM Therapy plus medical therapy (treatment) as compared to medical therapy alone (control). On January 8, 2024, we announced that the first patient was enrolled and randomized into the BACKBEAT study. We currently estimate completion of enrollment of the BACKBEAT study in mid-2026; however, there is no assurance that our current operating plan will be achieved. For a detailed description of the BACKBEAT study, see "*—BIOELECTRONIC PRODUCT CANDIDATES—AVIM Therapy for Hypertension and CNT-HF for Heart Failure—Clinical Results—Clinical, Regulatory and Commercialization Pathway—The BACKBEAT Global Pivotal Study."*

Virtue SAB

Virtue SAB is a proprietary drug/device combination product candidate for the treatment of artery disease that is designed to deliver a large liquid dose of proprietary, investigational, extended-release formulation of sirolimus ("SirolimusEFR") to the vessel wall during balloon angioplasty without the need for balloon coating or a permanent implant. Although the safety and efficacy profile has not yet been established by any regulatory body, Virtue SAB previously demonstrated promising three-year clinical data in the treatment of coronary ISR in the prospective, multi-center SABRE Study.

Virtue SAB was granted BDD by the FDA, for specific indications relating to the treatment of coronary ISR, coronary small vessel disease and peripheral artery disease below-the-knee. We estimate that these indications will represent an annual global addressable market opportunity of at least $10 billion, based on approximately 5 million procedures, as discussed below under *"—INTERVENTIONAL THERAPIES— Virtue SAB for Artery Disease and SirolimusEFR for Local Inflammation in Multiple Indications. — Targeted Unmet Needs and Market Opportunity for Virtue SAB."*

On April 29, 2025, we announced IDE approval from the FDA for the Virtue Trial, a pivotal trial to be conducted at up to 75 sites in the U.S. that is expected to randomize approximately 740 patients 1:1 to either treatment with Virtue SAB or Boston Scientific Corporation's AGENT™ paclitaxel-coated balloon (currently the only drug-coated balloon approved in the U.S. for a coronary indication) with a primary efficacy and safety endpoint of statistical non-inferiority of target lesion failure ("TLF") at 12 months post index treatment.

On October 27, 2025, we announced that we had initiated enrollment of patients for the Virtue Trial. We currently estimate completion of enrollment of the Virtue Trial in mid-2027; however, there is no assurance that our current operating plan will be achieved.

On October 28, 2025, we entered into a termination and right of first refusal agreement (the "Termination and ROFR Agreement") with Terumo Corporation and Terumo Medical Corporation (collectively, "Terumo") with respect to Virtue SAB. The Termination and ROFR Agreement, which supersedes and terminates the prior Virtue SAB distribution agreement between us and Terumo (the "Terumo Agreement"), grants Terumo a right of first refusal ("ROFR") to acquire the rights, or enter a distribution arrangement, with respect to Virtue SAB for the treatment of coronary artery disease, in exchange for an upfront payment of $10.0 million. For additional information relating to the Termination and ROFR Agreement, see the disclosure under the heading *"Termination and Right of First Refusal Agreement"* in Note 3 to the Consolidated Financial Statements included herein. In connection with the Termination and ROFR Agreement, on November 7, 2025, Terumo invested an additional $20.0 million in Orchestra BioMed through a new series of non-voting convertible preferred stock, par value $0.0001 per share (our "Series A Preferred Stock"), which is convertible into common stock in the future, subject to certain conditions, at a minimum of $12 per share pursuant to the terms of a securities purchase agreement (the "Terumo Securities Purchase Agreement"). Terumo previously made a $30.0 million non-refundable payment and $5.0 million common stock investment in Orchestra BioMed upon execution of the Terumo Agreement.

Ligand Pharmaceuticals Incorporated Revenue Participation Right Purchase and Sale Agreement and Purchase of Shares

On August 5, 2025, we announced that we had entered into a revenue participation right purchase and sale agreement (the "Revenue Purchase and Sale Agreement") with Ligand Pharmaceuticals Incorporated ("Ligand"). Under the terms of the Revenue Purchase and Sale Agreement, in exchange for payment of $35.0 million (the "Investment Amount"), less certain reimbursable expenses, Ligand acquired from us the right to receive tiered revenue payments (the "Revenue Interest") with respect to revenue (including certain licensing revenue) received by us in a calendar year in connection with worldwide net product sales, or other product revenue received by, by us and our licensees ("Annual Net Sales") of (a) AVIM Therapy (the "Primary Product") in the field of hypertension treatment and (b) the Virtue SAB (the "Secondary Product" and together with the Primary Product, the "Products") in the field of coronary artery treatment. Ligand also made a $5.0 million equity investment in the Company. For additional information, see Note 15 to the Consolidated Financial Statements – "*Royalty Purchase Agreement*."

History of Caliber and BackBeat

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

Conversion of Caliber and BackBeat Limited Liability Companies

On December 26, 2019, we completed the conversions of Caliber Therapeutics, Inc., a Delaware corporation, to Caliber Therapeutics, LLC, a Delaware limited liability company, and BackBeat Medical, Inc., a Delaware corporation, to BackBeat Medical, LLC, a Delaware limited liability company. References in this Annual Report on Form 10-K to "Caliber" refer to Caliber Therapeutics, Inc. prior to its conversion to a limited liability company and to Caliber Therapeutics, LLC after its conversion to a limited liability company, as applicable. References in this Annual Report on Form 10-K to "BackBeat" refer to BackBeat Medical, Inc. prior to its conversion to a limited liability company and to BackBeat Medical, LLC after its conversion to a limited liability company, as applicable.

Merger with Health Sciences Acquisitions Corporation 2

We were incorporated in the Cayman Islands in 2020, as a special purpose acquisition company under the name Health Sciences Acquisitions Corporation 2 ("HSAC2"). On January 26, 2023, Orchestra BioMed, Inc. and HSAC2 consummated a business combination with HSAC2 pursuant to which, among other things, Orchestra BioMed, Inc. became a wholly owned subsidiary of HSAC2 and HSAC2 changed its name to Orchestra BioMed Holdings, Inc. (the "Business Combination").

Partnership-Enabled Business Model

Our business was formed specifically to pursue a partnership-enabled business model that applies strategies typically used by the biopharmaceutical industry to the medical device market where product developers are often challenged with the financial and execution burdens of also commercializing the products they are developing to achieve a value inflection event for their shareholders.

Our goal is to accelerate and improve the likelihood of our product innovations reaching patients and providers worldwide by sharing the risks and rewards of developing and commercializing these product candidates with established multinational companies, such as Medtronic. Using this approach, we believe we can pursue multiple potentially lucrative innovation opportunities by focusing our efforts and resources on advancing promising therapeutic solutions, such as AVIM Therapy and Virtue SAB, through pivotal-stage clinical results. Meanwhile, our partners secure substantial new prospective growth opportunities with the potential to reduce risk and expense while leveraging their existing infrastructure to bring our partnered product candidates through regulatory approvals processes to global markets quickly and efficiently (assuming regulatory approval is obtained).

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

- ***Optimizing development and commercialization*** of product candidates by pairing its research and development strengths and capabilities with the established commercial infrastructure of our partners;
- ***Enhancing capital efficiencies*** by sharing costs and responsibilities with our partners; and
- ***Maximizing the potential of future profitability*** by seeking to create multiple long-term high-margin royalty and revenue sharing arrangements with our partners.

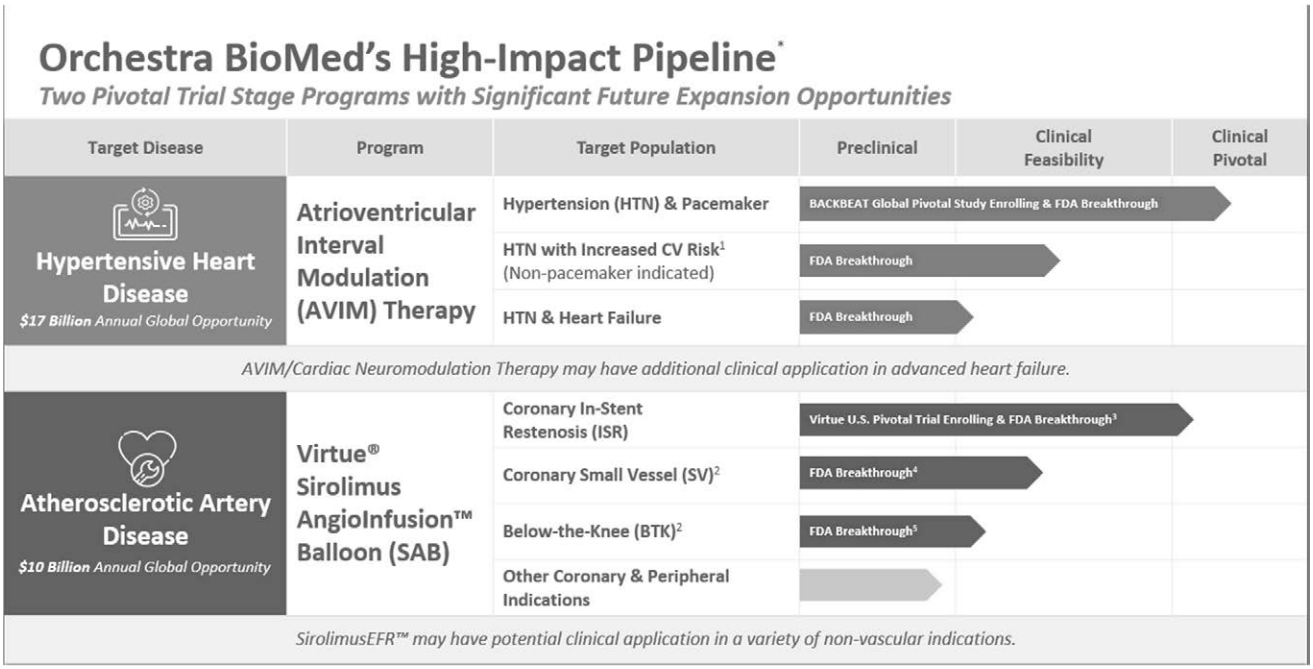
Our Product Pipeline

Our pipeline is comprised of innovative therapeutic product candidates that we believe have the potential for value creation using our partnership-enabled business model, led by our flagship technologies, AVIM Therapy and Virtue SAB. We believe our product pipeline has the potential to improve clinical outcomes and provide distinct commercial advantages major cardiovascular indications in large and well-established global medical device markets with unmet medical needs: AVIM Therapy in cardiac rhythm management implants, an overall global market that Grand View Research valued at a $17.2 billion market worldwide in 2024; and Virtue SAB in interventional devices to treat coronary artery disease ("CAD") and peripheral artery disease ("PAD"), an overall global market that IMARC Group, a leading market research company, valued at a $26.7 billion market worldwide in 2024. Our pipeline also includes additional product candidates for other significant medical conditions that we believe are attractive candidates for value creation using its partnership-enabled business model.

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

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

Advancing a High-Impact Pipeline



[1]Will seek to leverage data from the pilot and pivotal trials involving HTN in patients indicated for a cardiac pacemaker (the "HTN+P population" or the "Primary Field") to support clinical and regulatory development for HTN with high cardiovascular risk in patients not yet indicated for a pacemaker indication given that age and other demographic factors of the target population are expected to be similar, the type of hypertension treated will likely be isolated systolic hypertension which is predominant in the HTN+P population, and other co-morbidities are also expected to be common to both target populations.

[2]Plan to leverage existing coronary ISR data to support potential pivotal studies, although there have only been limited discussions with the FDA or comparable foreign regulators in this regard.

[3]Virtue SAB has received Breakthrough Device Designation by the FDA for the balloon dilatation of the stenotic portion (up to 26 mm length) of a stented coronary artery (ISR) that is 2.25 to 4.0 mm in diameter, for the purpose of improving lumen diameter.

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

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

BIOELECTRONIC PRODUCT CANDIDATES —AVIM Therapy for Uncontrolled Hypertension and CNT-HF for Heart Failure

We are developing bioelectronic therapies based on patented CNT technology. Our product candidates are designed to use standard active implantable cardiac rhythm management systems, such as pacemakers, with changes to firmware and software only. Our flagship product candidate of the Bioelectronic Therapies Group is AVIM Therapy, a patented, potential bioelectronic treatment for uncontrolled HTN, the leading risk factor for death worldwide. We have an exclusive strategic collaboration with Medtronic for the development and commercialization of AVIM Therapy for the treatment of uncontrolled HTN in patients indicated for a cardiac pacemaker. We also believe AVIM Therapy may offer therapeutic benefit to select patients with uncontrolled HTN who are not indicated for a pacemaker, including those with increased cardiovascular risk and HFpEF. Medtronic has a right of first negotiation with respect to AVIM Therapy for the treatment of HTN in non-pacemaker patients.

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

Atrioventricular Interval Modulation (AVIM) Therapy Product Candidate

In the discussion below and elsewhere in this Annual Report on Form 10 K, we reference p-values, which are statistical calculations that relate to the probability that the observed difference between groups happened by chance, with a p-value of less than 0.05 (i.e., less than a 5% probability that the observed difference happened by chance) generally considered as the threshold to indicate statistical significance in clinical trials.

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

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

Strategic Collaboration Agreement with Medtronic

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

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

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

Under the terms of the Medtronic Agreement, Medtronic will have exclusive rights in the Primary Field to commercialize AVIM-enabled pacing systems globally following receipt of regulatory approvals. Medtronic would be entirely responsible for global commercialization following any receipt of regulatory approvals, including manufacturing, sales, marketing and distribution costs. Under the terms of the Medtronic Agreement, assuming that AVIM-enabled devices are sold at average selling prices supported by existing reimbursement structures worldwide (e.g., no higher or additional reimbursement is available), we are expected to receive between $500 and $1,600 per AVIM-enabled device sold based on a formula of the higher of (1) a fixed dollar amount per AVIM-enabled device (amount varies materially on a country-by-country basis) or (2) a percentage of the AVIM Therapy generated sales. This estimated range is derived from publicly available information, our management's knowledge of the pacemaker market, our discussions with Medtronic, and the terms of the Medtronic Agreement. Based on our discussions with Medtronic, the global market leader in pacemakers, the terms of the Medtronic Agreement and our management's knowledge of reimbursement codes for medical devices, we believe that AVIM-enabled pacemakers can be supported by existing reimbursement codes without the need for new codes.

Under the terms of the Medtronic Agreement, Medtronic has a right of first negotiation through FDA approval of AVIM Therapy for the Primary Field, to expand its global rights to AVIM Therapy for the treatment of uncontrolled HTN in patients not indicated for a pacemaker.

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

On July 31, 2025, Orchestra BioMed, Inc., BackBeat and Medtronic entered into an amendment to the Medtronic Agreement, which became effective on August 4, 2025 (the "Medtronic Agreement Amendment"), to provide, among other things, a development and commercialization framework for future AVIM-therapy integration into a dual-chamber leadless pacemaker. Pursuant to the Medtronic Agreement Amendment, we will, among other things, be required to reimburse Medtronic for certain expenses incurred in connection with the integration of AVIM-therapy into Medtronic's dual-chamber leadless pacemaker, up to a specified cap.

Market Needs

Hypertension

HTN is elevated blood pressure that increases risk of major cardiac events like heart attack and stroke and can contribute to other significant conditions such as heart failure and kidney disease. According to the World Health Organization (the "WHO"), HTN is the leading global risk factor for death affecting an estimated 1.4 billion adults worldwide. Cardiovascular risk doubles for every 10 mmHg increase in office systolic blood pressure and the mortality rate doubles with an increase of 20 mmHg in office systolic blood pressure, according to the National Center for Biotechnology Information.

The Centers for Disease Control and Prevention (the "CDC") estimates 119.9 million adults, or approximately 48% of all adults in the United States have HTN. Within this group only 1 in 4 adults have their condition under control. In 2025, the American Heart Association ("AHA") and the American College of Cardiology ("ACC") updated their High Blood Pressure Clinical Practice Guideline, maintaining the same blood pressure thresholds established in 2017 for diagnosing hypertension—Stage 1 hypertension is defined as a systolic blood pressure of 130–139 mm Hg or diastolic blood pressure of 80–89 mm Hg, and Stage 2 hypertension as a systolic blood pressure of ≥140 mm Hg or diastolic blood pressure of ≥90 mm Hg. However, the 2025 guideline introduces new clinical tools and recommendations that further refine management strategies, including use of the PREVENT risk calculator to guide treatment decisions and broaden the indication for earlier pharmacotherapy in patients with Stage 1 hypertension who do not achieve targets with lifestyle changes. Under these updated guidelines, the estimated prevalence of hypertension among U.S. adults increased to nearly 47%, equivalent to approximately 120 million adults. While many global guidelines have not yet adopted these specific U.S. thresholds and continue to use the traditional ≥ 140/90 mmHg definition for diagnosing hypertension, the 2025 ACC/AHA guideline emphasizes more intensive control and earlier intervention to reduce cardiovascular and related risks. Importantly, a large proportion of U.S. adults over age 65—who are most likely to require pacemakers—now meet the criteria for hypertension under the updated definition. Additionally, the guideline recommends that a substantial number of U.S. adults taking antihypertensive medication may benefit from more intensive blood pressure–lowering treatment to achieve a target of <130/80 mmHg for optimal risk reduction.

The CDC reported high blood pressure as the primary or contributing cause of death in 2022 for more than 685,000 people in the United States, equating to nearly 1,875 deaths per day. By 2035, the estimated direct cost of high blood pressure could increase to $220.9 billion (annual average), according to the AHA.

Non-adherence to antihypertensive treatment is a critical contributor to suboptimal blood pressure control and another important risk factor for adverse cardiovascular disease outcomes. Of U.S. patients aware of their HTN diagnosis, about 76% are believed to be taking anti-hypertensive medication, but only 52% of those have their condition controlled, according to the Journal of Clinical Hypertension. Therefore, approximately 60% of hypertensive U.S. adults have uncontrolled HTN. An estimated 31% of HTN patients are non-adherent to medications, according to the AHA. Thus, many medically responsive patients have high blood pressure simply because they do not take their medications, making medication non-compliance one of the most prominent challenges of HTN management. In addition, since HTN patients are typically older, they are more likely to be prescribed multiple medications for HTN and other medical conditions: polypharmacy (multiple medications) is associated with increased risk of adverse events (fall injury, heart failure, etc.), polypharmacy mismanagement, and drug-drug interactions. Furthermore, AHA estimates as much as 15% of the prevalent HTN population is resistant to medical therapy, and these patients are 47% more likely to suffer the combined outcomes of death, myocardial infarction, heart failure, stroke, or chronic kidney disease over the median 3.8 years of follow-up than other HTN patients. Because of the factors mentioned above, there is a significant need for alternative therapies to treat HTN, particularly, device-based therapies that do not require patient compliance for receiving treatment.

Isolated Systolic Hypertension, Elevated Pulse Pressure & Diastolic Dysfunction

Based on data from the CDC, 72% of U.S. adults over 60 years old have HTN, with over 65% of them suffering from isolated systolic hypertension ("ISH"). ISH patients have elevated systolic blood pressure (>140 mmHg), while their diastolic blood pressure remains normal or low (≤90 mmHg). ISH is a more difficult to treat form of HTN because anti-hypertensive medications generally impact both systolic and diastolic pressure. It is estimated that over 80% of medical treatment failure patients over 60 years old have ISH, according to the AHA. ISH patients experience elevated pulse pressure, which is the difference between systolic and diastolic pressures ("Pulse Pressure"). Pulse Pressure is a known, significant, independent risk factor for coronary heart disease. According to published literature, a 10 mmHg increase in Pulse Pressure is associated with a 32% increase in risk of heart failure and a 24% increase in risk of stroke (after controlling for systolic BP and other risk factors). In addition, in men ≥60 years old (the typical age of pacemaker patients), risk for coronary artery disease is three times larger in patients with Pulse Pressure of ≥70 mmHg compared to those with Pulse Pressure of 60 mmHg.

Long standing HTN leads to cardiac structural and functional changes that frequently result in left ventricular ("LV") diastolic dysfunction ("DD"), a condition in which the left ventricle has impaired relaxation and filling, leading to increased pressure and reduced efficiency in pumping blood. It is a key contributor to heart failure with preserved ejection fraction (HFpEF), which accounts for approximately 50% of all heart failure cases. HTN is one of the primary causes of DD and the prevalence of DD increases with age, affecting over 50% of individuals over 70.

Hypertension among Patients with Pacemakers

Pacemakers are recommended for the management of symptomatic bradycardia (slow heart rate) due to sick sinus syndrome, atrio-ventricular block, a combination of these conditions or other situations in which patients are prone to brady-arrhythmias. Currently available devices have evolved from single-chamber, fixed-rate pacemakers to multi-chamber, rate-responsive units. In the United States, over 85% of pacemaker patients receive dual-chamber devices which have wires or leads implanted in the right atrium and right ventricle of the heart capable of sensing and stimulating the heart to control contraction timing of both chambers. There are projected to be approximately 1.4 million dual-chamber pacemaker implants performed worldwide in 2028 according to GlobalData & Life Science Intelligence. Global sales of dual-chamber pacemakers exceeded $3.6 billion in 2022 according to GlobalData, comprising over 20% of the overall $17.2 billion market for implantable cardiac rhythm management devices.

Based on ACC/AHA guidelines, we estimate that nearly 80% of U.S. patients that are indicated for the implant of a pacemaker have HTN. Among this group of patients, over 60% are estimated to have uncontrolled HTN based on the treatment goal per the 2025 ACC/AHA guidelines. Further, since the average age of pacemaker-indicated patients is approximately 73 years old and, in consideration of other demographic factors associated with this population, these patients are at elevated risk of ISH (over 80% of patients enrolled in prior clinical studies of AVIM Therapy had ISH). Furthermore, these patients are likely to suffer from DD, have increased overall cardiovascular risk as well as other co-morbidities such as atherosclerosis, hyperlipidemia, diabetes mellitus and chronic kidney disease. We believe these patients could benefit substantially from a HTN treatment like AVIM Therapy that can be administered via an already necessary pacemaker.

Target Patient Populations and Market Opportunity for AVIM Therapy

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

AVIM-enabled pacemakers can be implanted using standard implant procedures, electrical leads and lead positions. Further, we believe any experienced and trained physicians who perform pacemaker implants, such as electrophysiologists and cardiologists, will be able to select an AVIM-enabled pacemaker for an appropriate patient without the need for another physician referral, if approved. AVIM Therapy features proprietary algorithms that are designed to enable physicians to non-invasively adjust the therapeutic parameters to optimize chronic blood pressure reduction to individual patient needs. In addition, AVIM Therapy is designed to be de-activated or reactivated by the physician as necessary, offering potential efficacy and safety advantages over other device-based therapies. Importantly, the delivery of AVIM Therapy does not rely on patient adherence or compliance, offering a significant complement to pharmaceutical therapies for which adherence and compliance are a key challenge.

We estimate that the addressable annual market for pacemaker-indicated patients with HTN will comprise more than 1,000,000 patients worldwide by 2028. We estimate that, if approved, commercialization of AVIM Therapy in hypertensive pacemaker patients can increase the commercial value of the global pacemaker device market by over $2.4 billion annually. This substantial annual opportunity is based on incorporating AVIM Therapy's potentially potent and clinically impactful HTN treatment capabilities into a pacemaker to drive a meaningful increase in the average selling price ("ASP") that can be supported by existing pacemaker procedure codes globally.

AVIM Therapy may also offer clinical utility for HTN patients not yet indicated for a pacemaker who have uncontrolled systolic blood pressure despite medical therapy and have increased cardiovascular risk factors such as ISH, DD and additional serious medical comorbidities. We estimate that this additional addressable annual market for select patients with uncontrolled hypertension and high cardiovascular risk not yet indicated for a pacemaker will comprise at least 3.7 million patients worldwide by 2025, or approximately 0.2% of the global HTN population. We calculate this estimated market using information from publicly available third-party sources that only includes those hypertensive patients who are (1) over 60 years of age with high (>20%) ASCVD score, (2) are currently being treated with at least one medication, (3) have high systolic blood pressure (greater than 160 mmHg oSBP) despite medical therapy, (4) have preserved ejection fraction (EF >50%), (5) have ISH and/or DD or HFpEF, and (5) do not have high burden atrial fibrillation or severe valvular disease. Using similar maximum ASP figures based on existing reimbursement codes for pacemaker implantation, we estimate that this calculated market represents a global potential annual revenue opportunity of over $15.4 billion using similar potential ASPs as AVIM-enabled pacemakers.

FDA Breakthrough Device Designation

On April 22, 2025, we announced that the FDA had granted BDD for an implantable system for delivery of AVIM Therapy using conduction system pacing to reduce blood pressure in patients with preserved left ventricular systolic function and uncontrolled hypertension with increased high ten-year ASCVD risk, despite the use of anti-hypertensive medications or in patients who may have intolerance to anti-hypertensive medications. Orchestra BioMed estimates that there are over 7.7 million patients in the U.S. that meet the criteria for the BDD for AVIM Therapy.

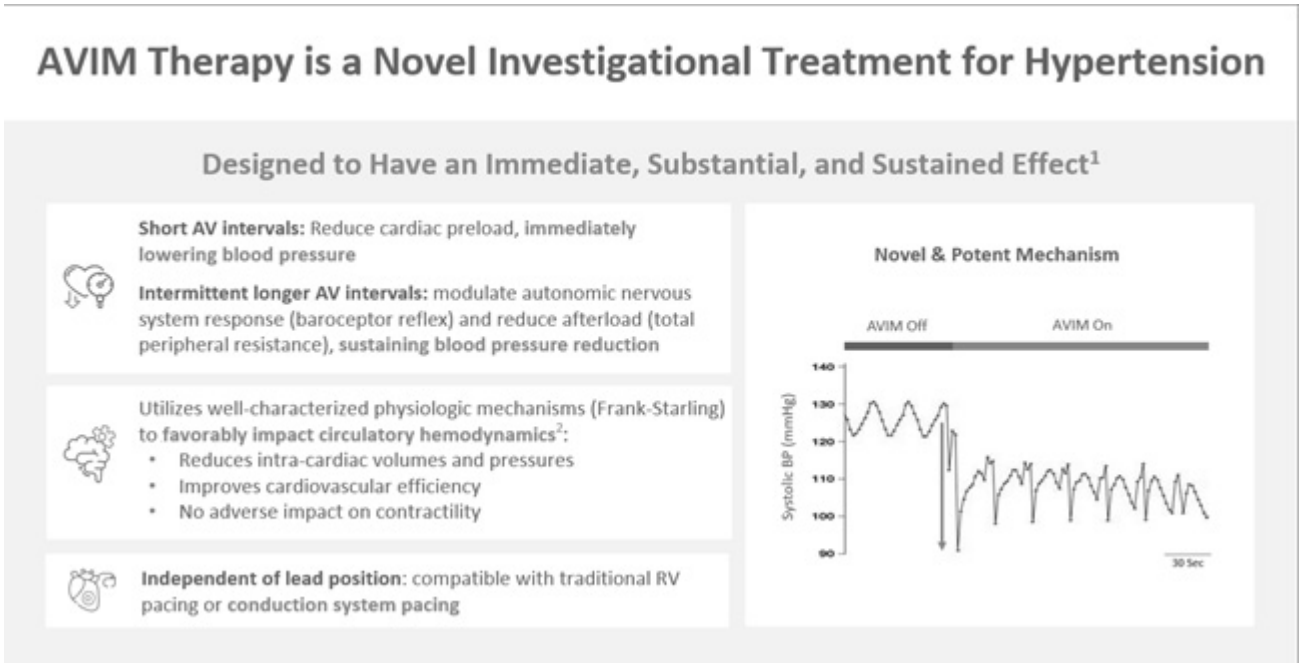
The FDA Breakthrough Devices Program, which reflects the FDA's commitment to device innovation and protecting public health, is designed to expedite the development and provide priority review of innovative medical technologies that have the potential to significantly improve outcomes for patients with serious or life-threatening conditions. To be eligible for this designation, a device must demonstrate the potential to provide more effective treatment or diagnosis of a life-threatening or irreversibly debilitating condition. In addition, the device must meet at least one of the following criteria: it must represent breakthrough technology, have no approved or clear alternatives, offer significant advantages over existing options, or be determined by the FDA to be in the best interest of patients. Beyond regulatory acceleration, the BDD may also support favorable reimbursement pathways, including eligibility for incremental inpatient reimbursement through the New Technology Add-on Payment ("NTAP") and outpatient Transitional Pass-Through payments ("TPT") under the Center for Medicare & Medicaid Services ("CMS") programs. These mechanisms may help facilitate more timely access to breakthrough technologies while supporting provider adoption and patient access.

Impact Potential of AVIM Therapy

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

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

1. Programmed pacing with short AV delays (shorter timeframe between contraction of the atria and the ventricle of the heart) designed to substantially reduce blood pressure by reducing cardiac preload. Cardiac preload is the amount of stretching of the ventricle of the heart driven by the volume of blood that fills the ventricle. Pacing with shorter AV delays reduces fill volume and, thereby, cardiac preload. Lower preload results in lower blood pressure.
2. Programmed variable blood pressure patterns (achieved using programmed pacing with a combination of short and intermittent longer AV delays) designed to maintain average blood pressure reduction by modulating sympathetic tone and reducing cardiac afterload. Sympathetic tone refers to the level of activity of the sympathetic nervous system response which is known to drive and maintain elevated blood pressures. Cardiac afterload is the vascular resistance against which the heart must contract to eject blood and is characterized by the diameter of arteries, otherwise known as total peripheral resistance.



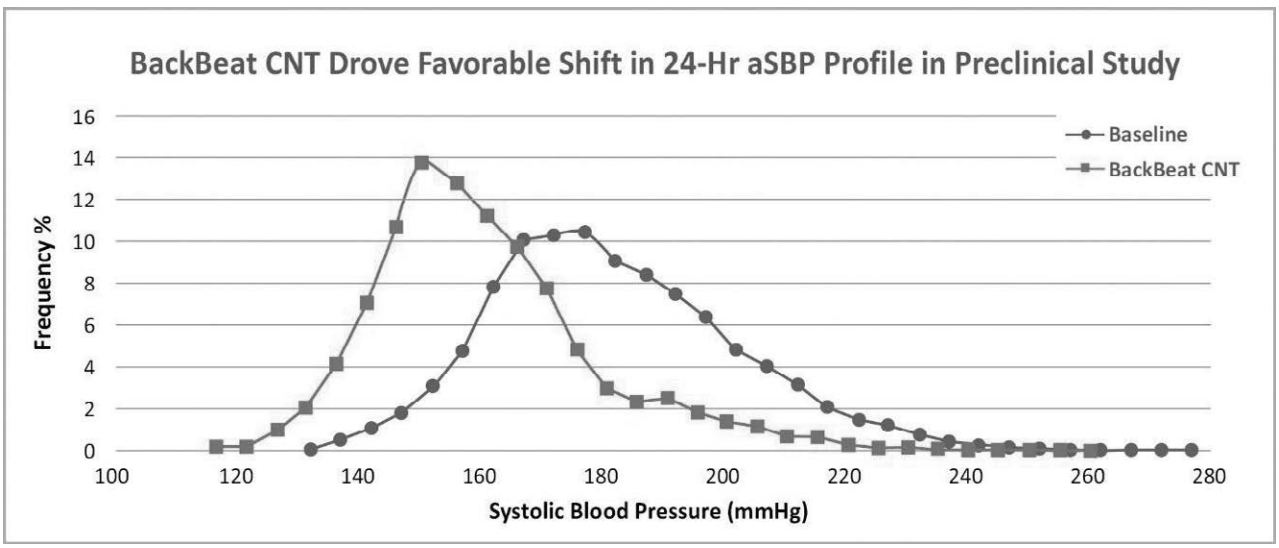
[1]Kalarus et al. Journal of the American Heart Association. 2021;10:e020492ahajournals.org/doi/10.1161/JAHA.120.020492.
[2]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24

Preclinical Data

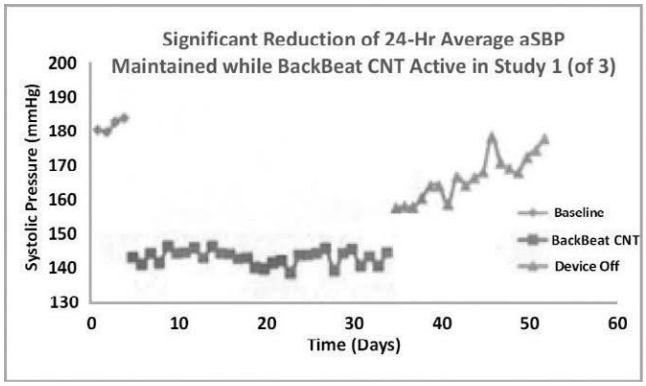
The goal of the preclinical studies was to evaluate the feasibility of the use of AVIM Therapy in a canine model with surgically induced HTN and to provide a rationale for clinical use to persistently lower blood pressure in patients with HTN. AVIM Therapy was delivered via pacing algorithms in a prototype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

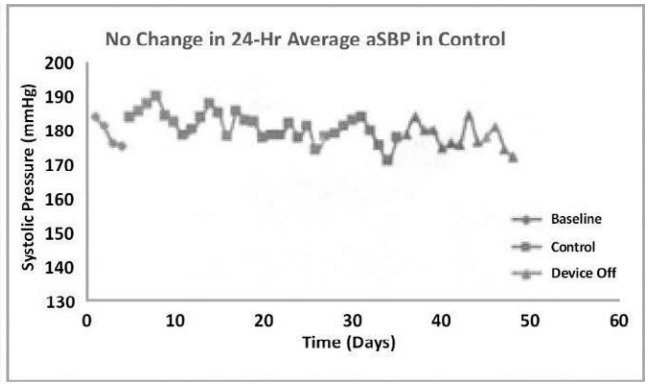
The reduction occurred immediately upon activation of therapy and was maintained for the period that the therapy was active (approximately 30 days). Blood pressure did not meaningfully change in the study's single control animal that had an AVIM Therapy device implanted but not activated. 24-hour aSBP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

The chart below shows the baseline 24-hour aSBP profile of one of the study animals prior to therapy activation as compared to the 24-hour aSBP profile of the same animal following activation of AVIM Therapy. The results are plotted as a histogram demonstrating the frequency of blood pressure levels over the course of the 24-hour period. The baseline aSBP histogram shows the percentage frequency of aSBP reaching different levels of pressure ranging from approximately 135 mmHg to 280 mmHg and a most frequent aSBP of approximately 180 mmHg. By contrast, the AVIM Therapy aSBP histogram shows the percentage frequency of aSBP reaching different levels of pressure ranging from approximately 120 mmHg to 260 mmHg and a most frequent aSBP of approximately 145 mmHg. The charts demonstrate the significant improvement in the entire 24-hour aSBP profile of the animal driven by AVIM Therapy as the entire aSBP histogram is shifted substantially downwards and to the left in terms of frequency of reaching lower SBP levels and the peak SBP frequency level is reduced by approximately 35 mmHg. These results are similar in the three AVIM Therapy study animals in terms of substantial improvement of the 24-hour aSBP profile while the one study control animal did not experience a shift in 24-hour aSBP profile.



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





Clinical Results

Acute Clinical Studies (Nanjing):

A short time-based study of the effects of AVIM Therapy in 18 patients with uncontrolled HTN who were already scheduled to undergo an invasive electrophysiology procedure was conducted at Jiangsu Province Hospital/The First Affiliated Hospital with Nanjing Medical University, Nanjing, China over a one year period ending March 2012. The study population consisted of patients with uncontrolled HTN and systolic blood pressure >140 mmHg despite at least one anti-hypertensive medication.

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

Acute Clinical Study (Prague):

On March 6, 2024, we announced the presentation of results from a pressure volume ("PV") loop clinical study of AVIM Therapy in pacemaker-indicated patients with uncontrolled HTN despite the use of anti-hypertensive medication. These clinical data demonstrate the favorable hemodynamic impact of AVIM Therapy as compared to standard right ventricular ("RV") pacing on systolic blood pressure and overall cardiac function when delivered using both conduction system as well as standard pacing lead locations. The PV loop study was conducted at Na Homolce Hospital in Prague by Petr Neužil, MD, CSc., FESC and the data were presented by Prof. Karl-Heinz Kuck, M.D., Medical Director at LANS Cardio Hamburg at the Technology and Heart Failure Therapeutics 2024 Meeting. On August 26, 2025, we announced that the results of this PV loop study were published in the *Journal of the American College of Cardiology: Clinical Electrophysiology*.

The PV loop study enrolled 16 patients indicated for a dual-chamber pacemaker that also had uncontrolled HTN despite taking anti-hypertensive medication who underwent invasive PV loop testing to evaluate cardiac function, measured by changes in LV volumes and pressures using a pressure-volume catheter placed in the LV. SBP was measured using a pressure transducer placed in the aorta, and baseline measurements were recorded using atrial pacing at a fixed rate. Normal conduction AVIM Therapy with pacing leads placed in AVIM RV locations, as well as in AVIM conduction system pacing (CSP) locations targeting the left bundle branch area (LBBA) regions, respectively, was compared to standard atrioventricular (AV) Pacing.

Overall mean results for each variable were calculated using paired measurements for each individual patient using AVIM RV, AVIM CSP and AV Pacing, respectively:

- AVIM Therapy generated statistically significant reductions ($p<0.05$) in systolic blood pressure (SBP), end diastolic volume (EDV), end diastolic pressure (EDP), and end systolic volume (ESV) using both AVIM RV and AVIM CSP pacing lead locations compared to AV Pacing
    - SBP was reduced by 17.1 mmHg and 19.2 mmHg compared to 1.6 mmHg
    - EDV was reduced by 12.6 mL and 18.6 mL compared to 1.4 mL
    - EDP was reduced by 2.3 mmHg and 3.6 mmHg compared to an increase of 0.3 mmHg
    - ESV was reduced by 11.0 mL and 14.1 mL compared to an increase of 1.8 mL
- AVIM Therapy drove statistically significant ($p<0.05$) reductions in stroke work (SW) without significantly reducing stroke volume (SV)
    - Stroke work (SW) was reduced by 1596 mL and 1870 mL compared to 42 mL
    - Stroke volume (SV) was not significantly reduced by AVIM RV, AVIM CSP or AV Pacing
- AVIM Therapy drove statistically significant ($p<0.05$) reductions in total peripheral resistance (TPR or Ea) and no change in contractility (Ees)
    - Effective arterial elastance (Ea, a measure of TPR) was reduced by 0.23 mmHg/mL and 0.31 mmHg/mL compared to an increase of 0.04 mmHg/mL
    - Ees remained unchanged with AVIM RV, AVIM CSP and AV Pacing

Chronic Clinical Studies:

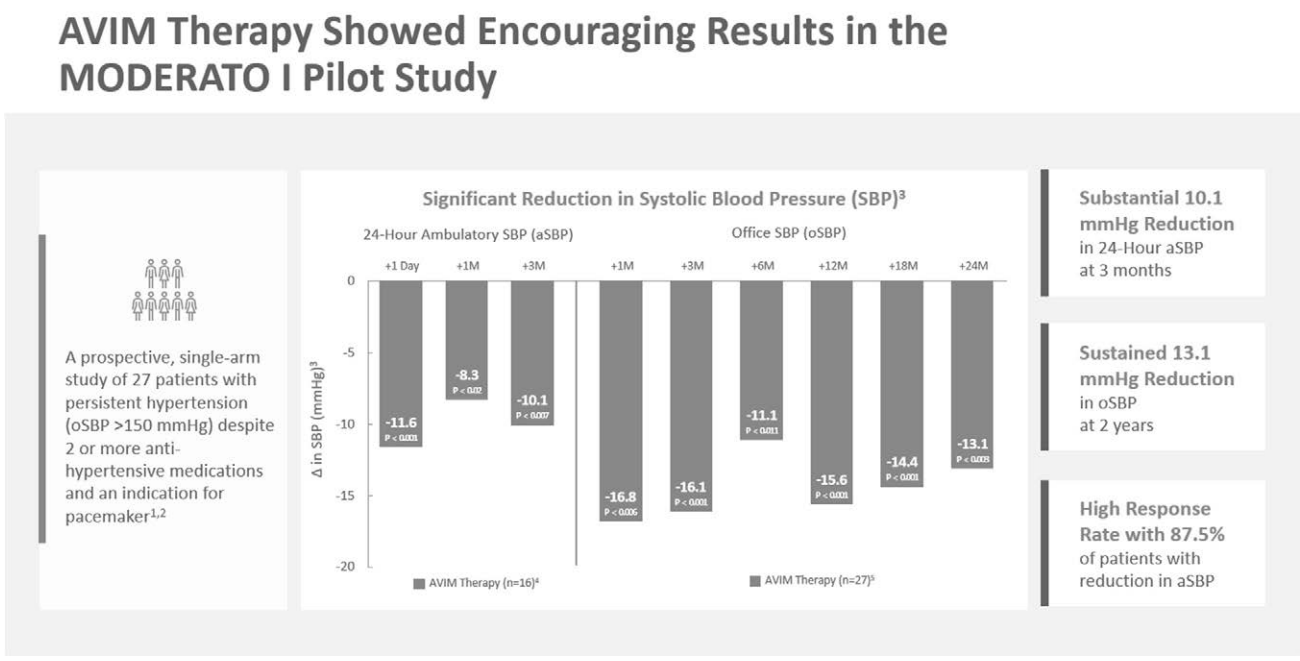
MODERATO I Single Arm Study

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

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

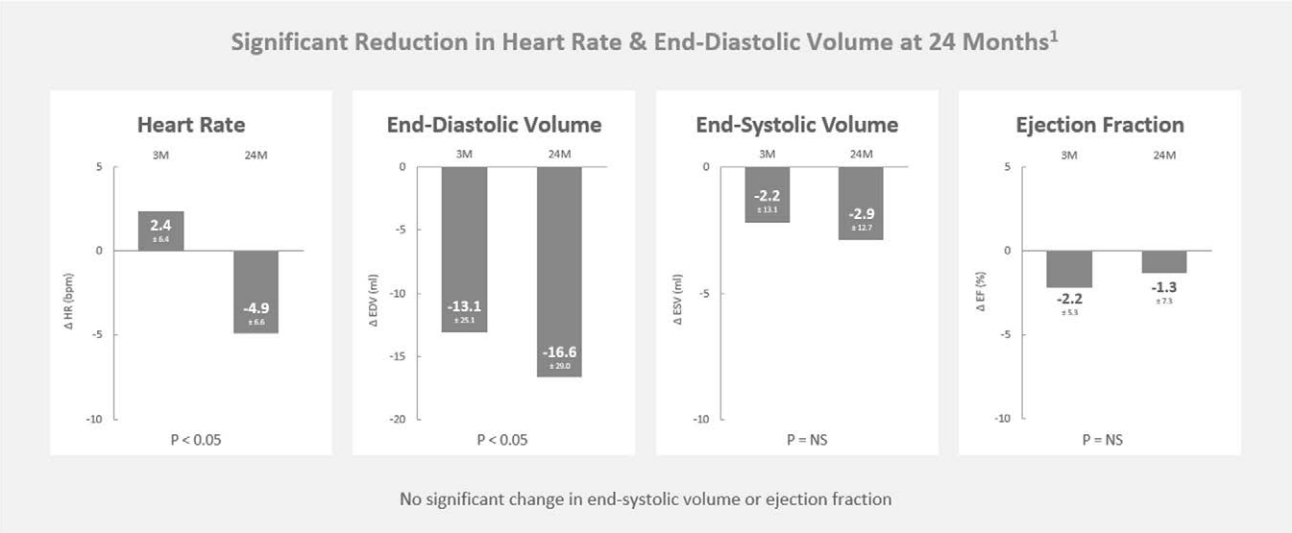
The co-primary efficacy endpoint of changes in mean 24-hour aSBP was met successfully with AVIM Therapy activation driving a significant 11.6 mmHg reduction ($p<0.001$) from pre-activation levels during the first day of therapy. The reduction was maintained through the three-month activation period,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

The co-primary efficacy endpoint of changes in oSBP was also met successfully with AVIM Therapy driving a statistically significant reduction in oSBP, 16.1 mmHg ($p<0.001$) from pre-activation levels. This reduction in oSBP was maintained in patients who reached the later follow-up time points with a mean statistically significant reduction of 23.4 mmHg ($p<0.001$) in oSBP from baseline levels after 24 months of therapy.



[1]Neuzil et al. *Journal of the Am Heart Assoc*. 2017;6:e006974.
[2]Burkhoff MODERATO I Study 2-Year Results TCT 2018.
[3]Compared to pre-activation.
[4]aSBP (n=16) at pre-activation.
[5]AVIM (n=21) continued after completion of study at 3 months to be followed for 2 years.

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



[1]Burkhoff MODERATO I Study 2-Year Results TCT 2018.

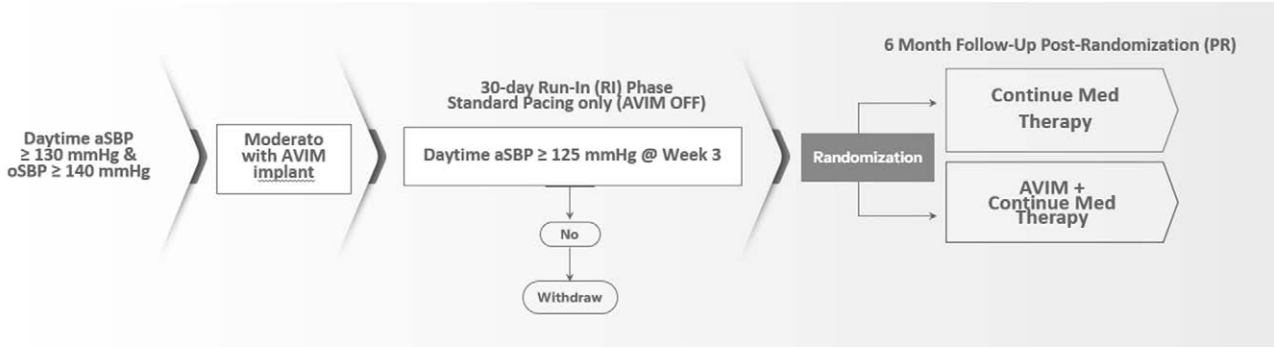
24-month Data Consistent with Expected Mechanism of Action

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

During the extended 21-month follow-up period that included 24 patients who continued with AVIM Therapy, there were 25 SAEs in twelve patients. No events were adjudicated as definitely or probably related to AVIM Therapy. Out of 25 events, 17 events in seven patients were cardiac related. There were eight non-cardiac events in eight patients. The non-cardiac events included two orthopedic events, two cases of cancer, a transient ischemic event, and three respiratory related events. Five events in three patients were adjudicated as possibly device related. These included two events of atrial fibrillation in the same patient, pneumonia with cardiac decompensation and dyspnea with cardiac decompensation in one patient, and cardiac decompensation in another patient.

MODERATO II Double-Blind, Randomized Study

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



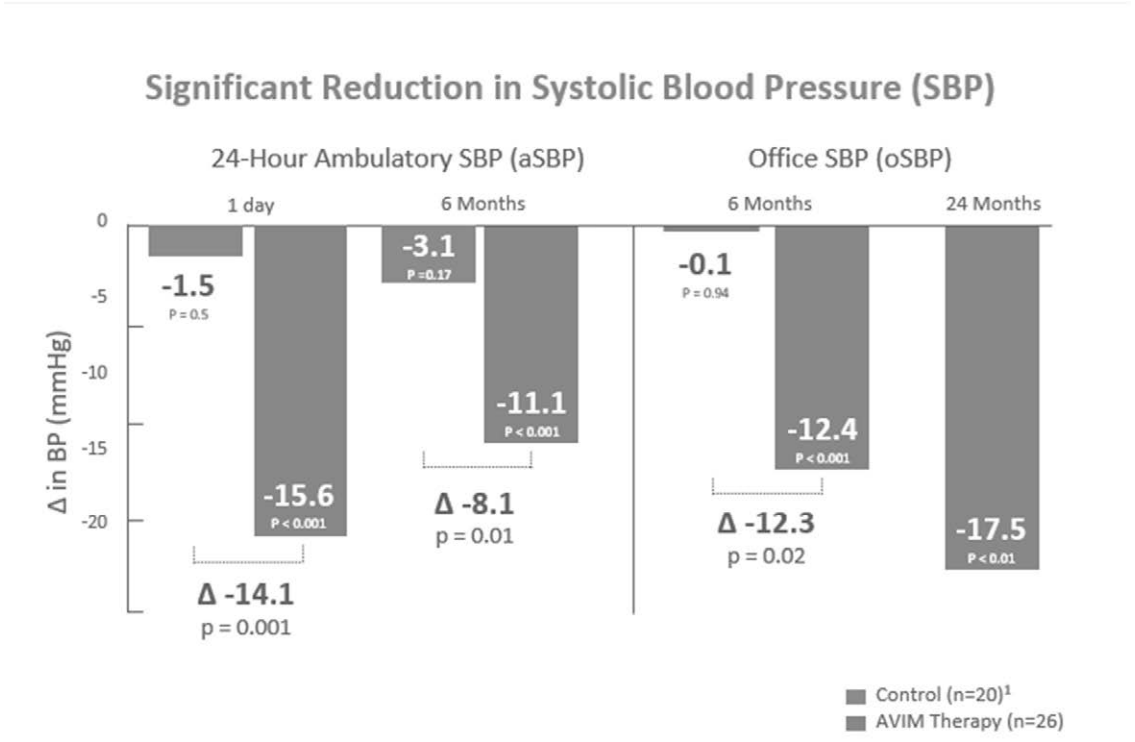
Prior to randomization, mean aSBP for both groups was 136.3 mmHg with patients, on average, treated with over three prescribed anti-hypertensive drugs. 88.5% of the patients in the AVIM Therapy treatment arm had ISH, making them a more challenging group of patients to treat. 71.4% of control arm patients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

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

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

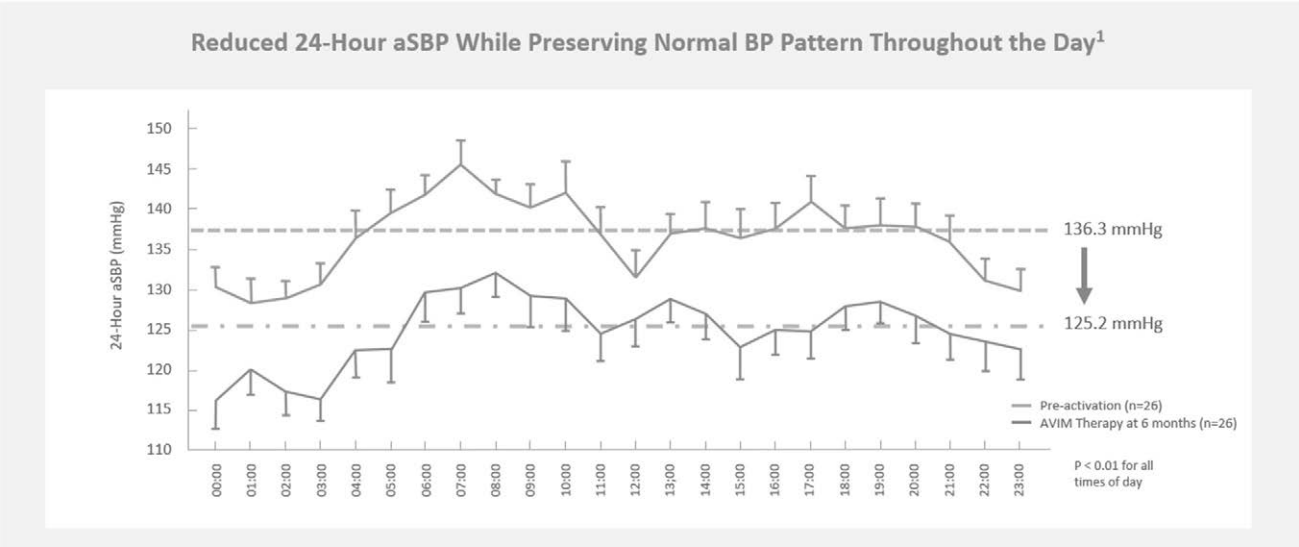
The MODERATO II study also met its primary safety endpoint, which was no significant differences in rates of MACE. There were no MACE in the AVIM Therapy group and three MACE in two patients in the control group (one death from cancer and two cardiac events) at six months. Additionally, there were no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

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



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

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



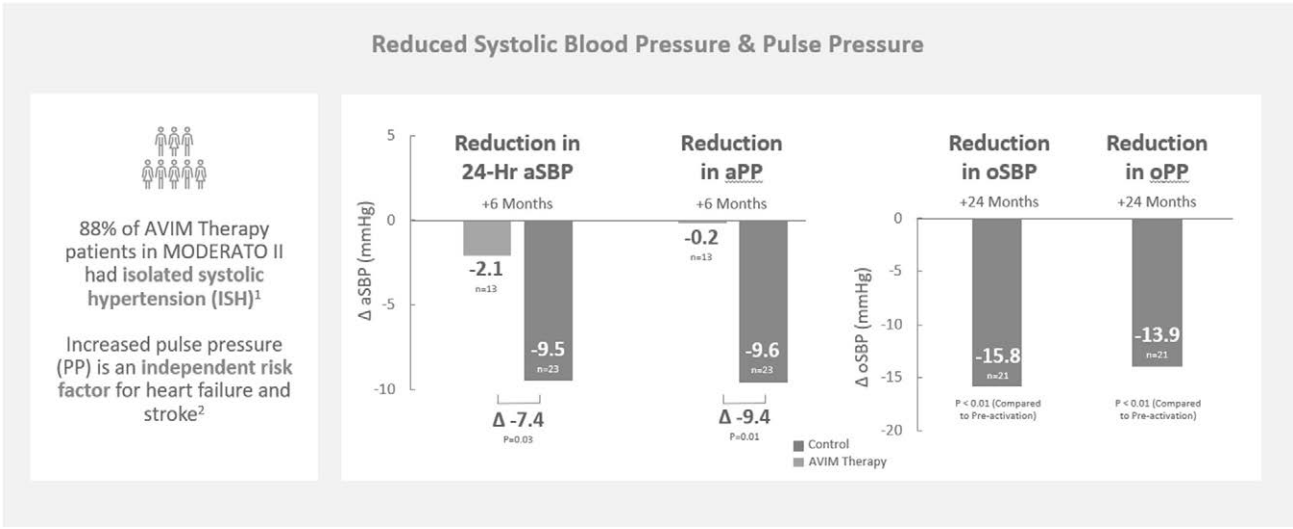
Source: 1Burkhoff MODERATO II Study 2-Year Results TCT 2021.

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

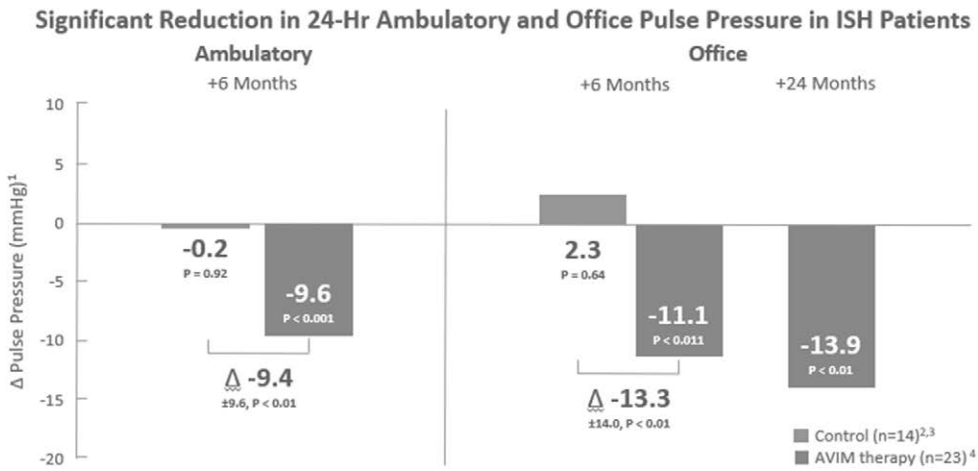
- Statistically significant mean reductions in aSBP (-10.3±9.3 mm Hg, $p<0.01$) and ambulatory pulse pressure (-11.7±5.5 mmHg, $p<0.01$) at six months post therapy activation compared to pre-crossover.
- Minimal changes in mean ambulatory diastolic blood pressure (+1.5±5.5 mmHg, p=NS) at six months post therapy activation compared to pre-crossover.
- Mean oSBP decreased by 13.1±26.6 and 13.8±28.7 mmHg at six and eighteen months post therapy activation, respectively, compared to pre-crossover.

MODERATO II Results in ISH Patients

In a subgroup of the MODERATO II study's patients with ISH, a dangerous and challenging to treat form of HTN prevalent in older patients, treatment with AVIM Therapy resulted in clinically meaningful and statistically significant reductions of 7.4 mmHg in aSBP and 11.9 mmHg in oSBP when compared to control (continued medical therapy) patients at six months. Further, in patients with ISH, AVIM Therapy drove statistically significant reductions of 9.4 mmHg in ambulatory Pulse Pressure and 13.3 mmHg in office Pulse Pressure at six months as compared to control patients.



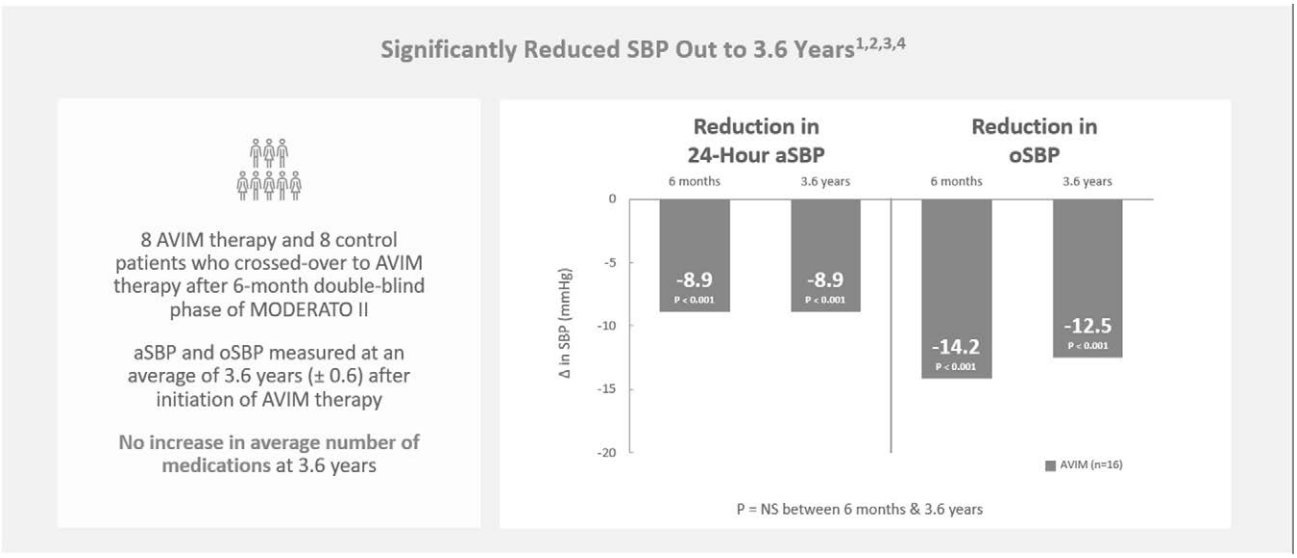
[1]Burkhoff MODERATO II Study 2-Year Results TCT 2021.
[2]Vaccarino V, et al. Am J Cardiol. 2001.
Definitions: aPP = ambulatory Pulse Pressure, oPP = office Pulse Pressure



[1]Compared to pre-activation.
[2]24-Hr Ambulatory Pulse Pressure control (n=13) at 6 months. One died of cancer, and one had unsuccessful recording.
[3]Office Pulse Pressure control (n=14) at 6 months. One died of cancer.
[4]AVIM Therapy(n=21) at 24 months. One died of cancer, and one died from Covid-19.

MODERATO II Long-Term Follow Up & Therapy Washout Study:

On February 26, 2024, we announced new data demonstrating sustained, clinically meaningful reduction in 24-hour ambulatory systolic blood pressure (aSBP) in hypertensive pacemaker patients treated with AVIM Therapy for over 3 years. Reduction in aSBP measured at 6 months from randomization and therapy activation was the primary endpoint of the MODERATO II study, a European multi-center, double-blind, randomized pilot study involving 47 subjects. Patients randomized to AVIM Therapy and antihypertension medication in that study experienced an 11.1 mmHg ($p<0.001$) reduction in mean aSBP at 6 months follow-up, resulting in a statistically significant difference of 8.1 mmHg compared to control patients who were managed only with anti-hypertensive medications ($p=0.01$). Long-term blood pressure results are from a follow-up study of 16 patients originally enrolled in the MODERATO II study. This group included eight patients from the MODERATO II study's AVIM treatment arm and eight control arm patients that crossed over to AVIM Therapy at the end of the 6-month double-blind phase. In this group of patients, aSBP was measured, on average, 3.6 (±0.6) years following initiation of AVIM Therapy. As a group and based on individual paired data, these patients continued to experience a statistically significant, clinically meaningful mean aSBP reduction of 8.9 mmHg at long-term follow up, which is similar to the mean aSBP reduction of 8.9 mmHg seen in this same group of patients when measured at the 6-month aSBP measurement.



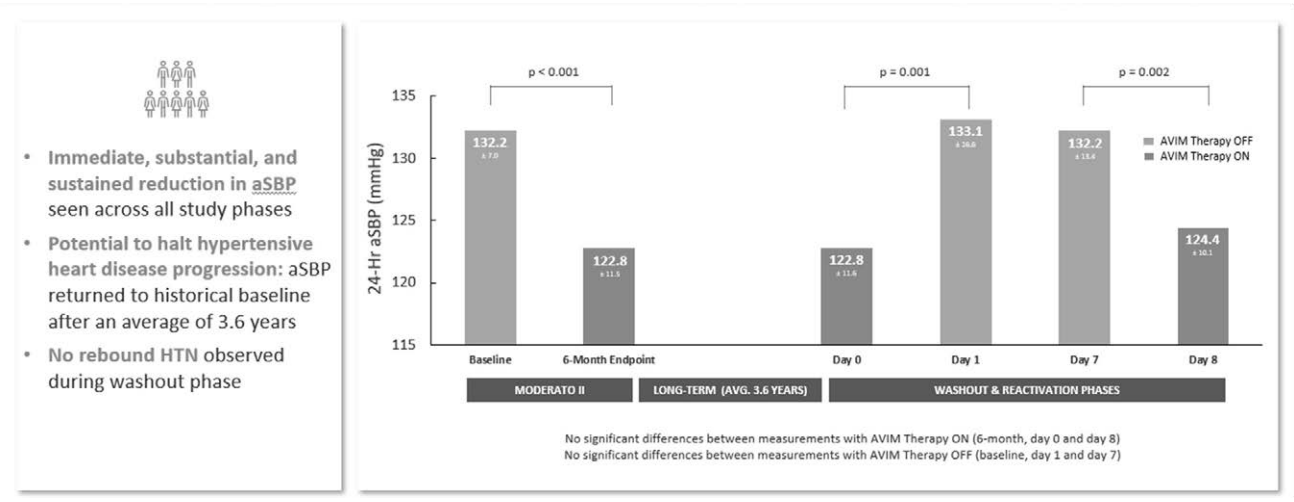
[1]Kalaras et al. Journal of the American Heart Association. 2021;10:e020492 ahajournals.org/doi/10.1161/JAHA.120.020492.
[2]Burkhoff MODERATO II Study 2-Year Results TCT 2021.
[3]Fischer MODERATO Study Long-term Results ICI 2024.
[4]Patients re-consented for long-term follow-up.

On September 4, 2025, we announced the presentation of additional clinical results at the HRX Live 2025 Meeting, in Atlanta, GA, demonstrating that the sustained blood pressure-lowering effects of AVIM Therapy are reversible with no evidence of rebound hypertension or blood pressure exceeding initial baseline values, and can be restored upon reactivation. These data further support AVIM Therapy's potential role as a controllable, programmable, and durable device-based therapy for uncontrolled hypertension. Key findings included:

- **Reversible treatment effect following therapy deactivation:**
  - Return to baseline: AVIM Therapy was turned off for a washout period of seven days. On Day 1, aSBP returned to 133.1 mmHg, consistent with original baseline hypertension (132.2 mmHg; p=NS).
  - Absence of rebound hypertension: No residual antihypertensive effects or rebound hypertension were observed.

- **Immediate effect upon therapy reactivation:**
  - Restored reduction in aSBP: Following the 7-day washout period, aSBP was immediately and significantly reduced (124.4 mmHg; $p<0.002$) upon reactivation.

- **Reproducible effect:**
  - No statistically significant difference in the therapeutic effects of AVIM Therapy were observed between 6-month (122.8 mmHg), chronic 3.6-year follow-up (122.8 mmHg) and Day 8 reactivation (124.4 mmHg).



MODERATO II Results in Patients with Diastolic Dysfunction

In February 2025, we announced results from a retrospective analysis of the MODERATO II study's data demonstrating favorable impact of AVIM Therapy on Echo markers of diastolic dysfunction ("DD"), a key driver of heart failure progression. The results were presented as late-breaking science at the Technology and Heart Failure Therapeutics ("THT") 2025 Conference. HTN is the leading cause of DD; both conditions are common in older patients and contribute to the development of heart failure. On August 15, 2025, we announced that these results were published in the *Journal of the American College of Cardiology: Advances.*

The retrospective, treatment-blinded analysis of the MODERATO II study assessed the impact of 6 months on systolic blood pressure ("SBP") and Echo markers of DD using core lab Echos with independent blinded adjudication. Patients were classified as with DD ("DD+") or without DD ("DD-") using the American Society of Echocardiography Guidelines. From the MODERATO II study cohort (n=47), 36 patients had technically sufficient Echo data, and 61% of this group (22/36) had Echo evidence of DD.

Using key measures of diastolic function, AVIM Therapy:

- **Significantly reduced office and ambulatory SBP in patients with DD through 6 months**
  - Ambulatory SBP ("aSBP") was reduced in AVIM-treated DD+ patients (N=12) by 8.3±9.7 mmHg ($p<0.01$ vs. baseline) compared to 2.2±9.8 mmHg in the control DD+ group (N=10)
  - Office SBP ("oSBP") was reduced in AVIM-treated DD+ patients by 12.1±12.8 mmHg ($p<0.01$ vs. baseline) compared to an increase of 2.9±26.4 mmHg in the control DD+ group (N=10)
  - SBP reduction was similar in patients with and without DD

- **Significantly improved key measures of diastolic dysfunction**
  - In patients with DD, AVIM Therapy demonstrated favorable Echo changes consistent with improved myocardial relaxation and diastolic compliance. Specifically, in comparison to DD+ control patients, AVIM-treated DD+ patients experienced a significant increase in e' (from 5.9±2.0 to 8.8±3.4cm/sec; $P<0.01$) consistent with an improvement in left ventricular relaxation and a significant increase in E/A (from 0.86±0.39 to 1.60±0.84; $P<0.01$) consistent with improved passive filling of the left ventricle despite reduced filling time (the designed effect of AVIM Therapy) with no significant changes in left atrial size.

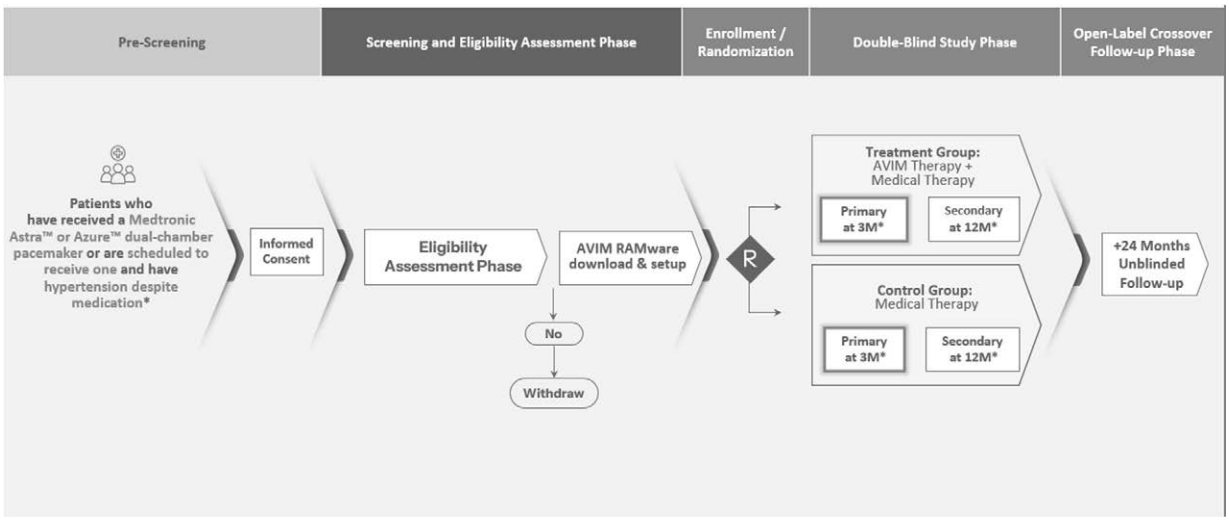
These findings provide further evidence that AVIM Therapy, in addition to significantly reducing systolic blood pressure, may also favorably influence ventricular function in important ways for patients with DD and at risk for heart failure.

Clinical, Regulatory and Commercialization Pathway

The BACKBEAT Global Pivotal Study

On September 19, 2023, we announced that the FDA granted us IDE approval to initiate our planned BACKBEAT study to treat uncontrolled HTN in patients indicated for a pacemaker. On January 8, 2024, we announced that the first patient was enrolled and randomized into the BACKBEAT study in late December 2023. The BACKBEAT study is a global, multi-center, prospective, randomized, double-blind study investigating the efficacy and safety of AVIM Therapy in patients who have recently undergone implantation of a Medtronic dual-chamber cardiac pacemaker and have uncontrolled HTN despite the use of anti-hypertensive medications. We are actively screening patients for enrollment in the BACKBEAT study. Site activations are expected to continue throughout 2025 with a target of activating up to 130 centers in the United States and Europe. The study will randomize up to 500 patients 1:1 to AVIM Therapy combined with continued medical therapy (treatment) or continued medical therapy and standard pacing alone (control). The study's primary efficacy endpoint will determine at three months post-randomization whether AVIM-treated patients experience a statistically significant reduction in daily average blood pressure (mean 24-hour aSBP) as compared to control patients. The primary safety endpoint will determine at three months post-randomization whether AVIM-treated patients experience serious adverse device effects that are not anticipated with cardiac pacing. Double-blind follow-up will continue through 12 months to enable the collection of additional clinical endpoints. All patients will be eligible to cross over upon completion of the 12-month blinded follow-up phase. The updated protocol also streamlines site coordinator and patient visit activities. We currently estimate completion of enrollment of the BACKBEAT study in mid-2026; however, there is no assurance that our current operating plan will be achieved.

The design of the BACKBEAT study is outlined in the chart below:



We utilize a four-pronged approach to support clinical activities for the BACKBEAT study: (1) full-time employees and consultants to directly manage the study in Europe; (2) U.S. based full-time employees who manage and oversee clinical trial work that is outsourced to contract research organizations (CROs), strategic partners, and service vendors, including site management and safety monitoring activities; (3) regional field clinical engineers ("FCEs") who support site activations and on-site clinical activities in the U.S. and Europe, including AVIM programming support ; and (4) FCE and other clinical and regulatory resources from Medtronic, our strategic partner, to assist with certain clinical study activities.

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

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

AVIM Therapy & CNT-HF for Heart Failure

Our Bioelectronic Therapies group is also seeking to develop a pipeline of additional treatments for development and future licensing based on its patented CNT technology. The lead follow-on therapy candidate is CNT-HF, a bioelectronic treatment for HF. According to the AME Medical Journal, HF affects an estimated 64 million people worldwide. According to the Journal of Cardiac Failure, 6.7 million Americans have HF costing nearly $31.0 billion annually. AHA projects the cost of HF will increase by 127% to $69.8 billion in 2030, amounting to approximately $244 for every U.S. adult. Heart failure was a contributing cause of death in the U.S., resulting in over 400,000 deaths in 2022 and accounted for about 45% of cardiovascular deaths that year, according to the Heart Failure Society of America. Approximately half of the patients with signs and symptoms of heart failure have largely normal left ventricular ejection fraction and are therefore considered Heart Failure patients with Preserved Ejection Fraction ("HFpEF"), according to the AHA. The prevalence of HFpEF compared with prevalence of HF with reduced ejection fraction ("HFrEF"), appears to be increasing over time along with aging of the population and the increasing prevalence of risk factors for HFpEF, such as obesity, HTN, and type 2 diabetes as well as improvements in diagnosis, according to the AHA. Those living with HFpEF experience frequent hospitalizations and high mortality rates. Nevertheless, there are currently no approved disease-modifying therapies for HFpEF. The success of existing HF therapies is mostly limited to treatment of HFrEF, not HFpEF, according to GlobalData.

We are exploring the benefits of AVIM Therapy in patients with HTN and/or ISH that are at high risk for the development of HFpEF or have early-stage HFpEF. We believe there is a likely physiological relationship between chronic HTN, particularly ISH, and other conditions such as DD, and the development of HF. We believe AVIM Therapy may play a beneficial role in the dynamic, helping to prevent progression of HFpEF. We are planning to initiate a pilot clinical study in 2026 of AVIM Therapy for the treatment of patients with HFpEF using our proprietary Moderato Plus IPG.

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

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

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

We are developing high impact therapeutic product candidates designed to optimize focal drug delivery during well-established interventional procedures with the objective of improving clinical outcomes and reducing complications. Our flagship product candidate of the Interventional Therapies portfolio is Virtue SAB, a drug-device product candidate that is designed to enable targeted delivery of sirolimus, an approved pharmaceutical agent for preventing restenosis during interventional stent treatment of artery disease, the leading cause of death worldwide. We are also exploring multiple additional applications of SirolimusEFR, our proprietary, investigational extended focal release formulation of sirolimus used in Virtue SAB. Sirolimus is a widely used anti-proliferative, anti-inflammatory pharmaceutical. We believe its unique formulation has the potential for the treatment of local inflammation in target tissues other than coronary and peripheral arteries, and a broad array of additional indications in which we are conducting early exploratory work, such as urology.

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

Virtue Sirolimus AngioInfusion Balloon

Virtue SAB is a novel, proprietary drug-device combination product candidate for the treatment of artery disease that is designed to deliver a large liquid dose of extended focal release formulation of sirolimus to the vessel wall during balloon angioplasty without the need for balloon coating or a permanent implant. Virtue SAB utilizes two key enabling technologies, our proprietary, investigational formulation of sirolimus, SirolimusEFR, and its patented microporous AngioInfusion Balloon, that work synergistically to optimize the clinical performance of the product candidate. Virtue SAB demonstrated promising clinical data from the SABRE trial, a multi-center, prospective, independent core lab-adjudicated pilot clinical study of 50 patients with coronary ISR conducted in Europe. We are currently enrolling patients in the Virtue Trial, a U.S. IDE pivotal trial to be conducted at up to 75 sites that is expected to randomize approximately 740 patients 1:1 to either treatment with Virtue SAB or Boston Scientific Corporation's AGENT™ paclitaxel-coated balloon (currently the only drug-coated balloon approved in the U.S. for a coronary indication) with a primary efficacy and safety endpoint of statistical non-inferiority of target lesion failure ("TLF") at 12 months post index treatment. The aim of this study is to support regulatory approval of Virtue SAB in the U.S. and other countries around the world. We believe Virtue SAB has the potential for further evaluation in follow-on clinical indications such as treatment of de novo coronary small vessel ("SV") disease, below-the-knee peripheral disease ("BTK"), and other therapeutic areas such as urology.

Termination and ROFR Agreement with Terumo

On October 28, 2025, we entered into the Termination and ROFR Agreement with Terumo with respect to Virtue SAB. The ROFR Agreement, which supersedes and terminates the Terumo Agreement, grants Terumo a ROFR to acquire the rights, or enter a distribution arrangement, with respect to Virtue SAB for the treatment of coronary artery disease, in exchange for an upfront payment of $10.0 million. In connection with the Termination and ROFR Agreement, on November 7, 2025, Terumo invested an additional $20.0 million in Orchestra BioMed through our Series A Preferred Stock, which is convertible into common stock in the future, subject to certain conditions, at a minimum of $12 per share. Terumo previously made a $30.0 million non-refundable payment and $5.0 million common stock investment in Orchestra BioMed upon execution of the Terumo Agreement.

Market Needs — Coronary and Peripheral Artery Disease

Artery disease is caused by atherosclerosis, the hardening and narrowing of the arteries due to the build-up of fatty material and plaque that reduces blood flow through the blood vessels supplying the heart muscle (coronary artery disease or "CAD") or limbs (peripheral artery disease or "PAD"). CAD reduces blood flow and oxygen supply to the heart muscle and can result in angina, heart attack and lead to heart failure and arrhythmias. PAD can happen in any blood vessel, but it is more common in the legs than the arms and can lead to pain, muscle weakness, wounds and ulcers that are difficult to heal and, eventually, amputation.

According to the WHO, cardiovascular diseases are the top cause of global death, resulting in over 19.8 million deaths annually worldwide. The CDC estimates 1 in 20 adults (approximately 5%) in the U.S. aged 20 and older have CAD and reported 370,000 CAD-driven deaths in the United States in 2022.

The AHA also estimates 10-12 million adults in the United States have PAD, including up to 15% of individuals older than age 70.

Interventional Cardiology

Interventional cardiology is a medical specialty that uses minimally invasive transcatheter, percutaneous technologies and techniques to treat artery disease and atherosclerosis. Catheter-based interventions using balloon angioplasty, stents and other technologies are the most common medical procedures used to treat artery disease and related conditions. There were over 6.4 million coronary and over 1.6 million peripheral catheter-based interventional procedures performed worldwide in 2022 according to Global Data & LSI Research. The global market for coronary interventional devices used to treat CAD, such as stent and balloon angioplasty systems, was valued at approximately $27.8 billion in 2024, and the global market for devices used to treat PAD, including angioplasty balloons, drug-coated balloons ("DCBs"), stents and atherectomy systems, was valued over $7.8 billion in 2022, according to market research firms Grand View Research and Straits Research.

The Evolution of Available Treatment Options

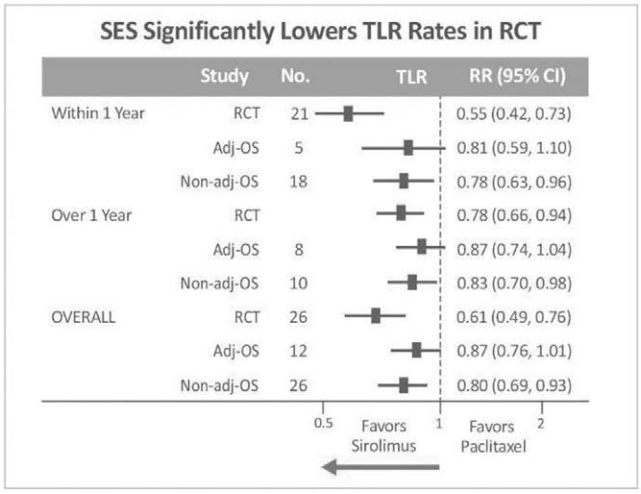
Balloon angioplasty is a procedure where small balloons integrated into catheters are introduced into the vascular system through a small puncture in the femoral artery in the leg or radial artery in the arm. Using specialized imaging technology called angiography, the balloon catheter is threaded through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

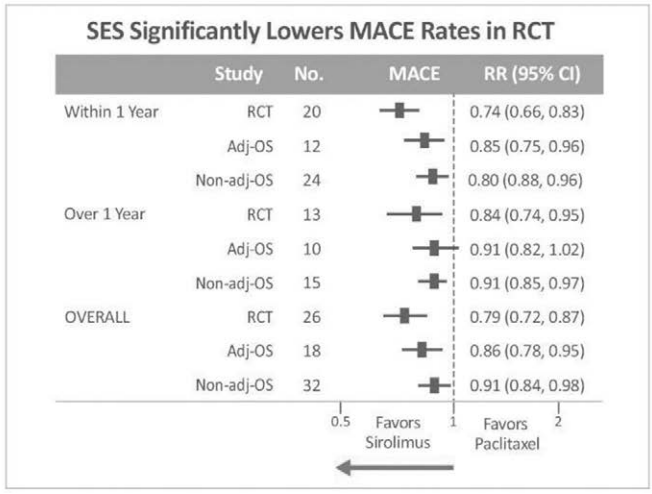
While plain balloon angioplasty can offer significant clinical benefits, it also comes with drawbacks, such as elastic recoil, arterial remodeling or vascular smooth muscle cell excessive proliferation resulting in restenosis (vessel renarrowing) in response to balloon injury. These problems drove the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

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

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

In a large meta-analysis of 76 studies in patients undergoing percutaneous coronary intervention, 'limus-eluting stents outperformed paclitaxel-eluting stents. In a meta-analysis of 26 randomized controlled trials ("RCTs"), 'limus-eluting stents demonstrated superior safety and efficacy with significantly lower MACE and target lesion revascularization, rates compared to paclitaxel-eluting stents (see figures below). Thus, 'limus analog eluting stents have become the clear "gold standard," with nearly 100% current global market share in the coronary DES marketplace.

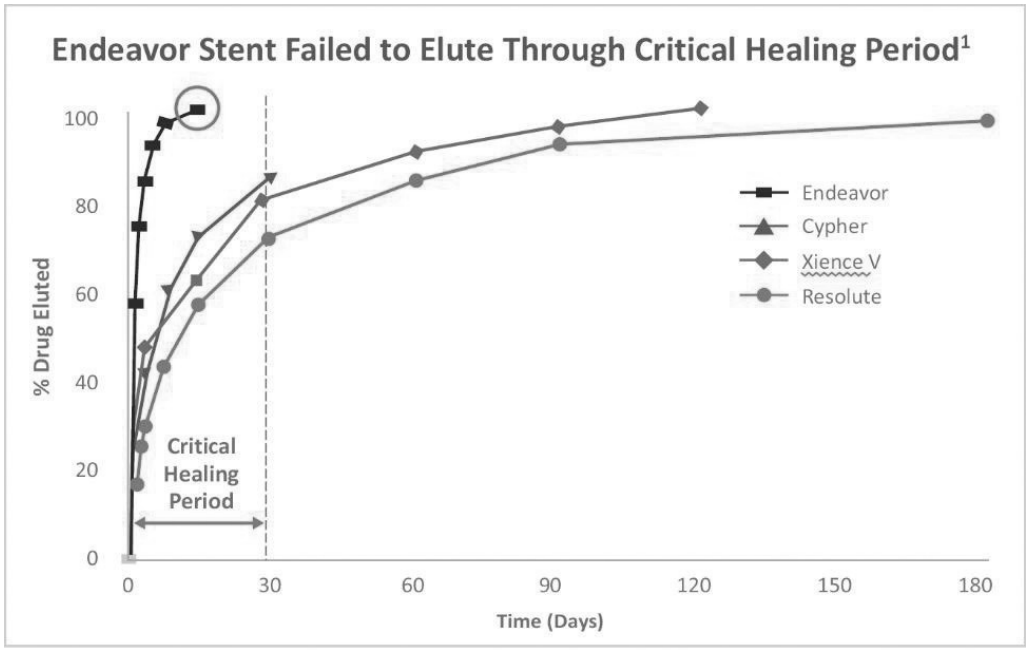


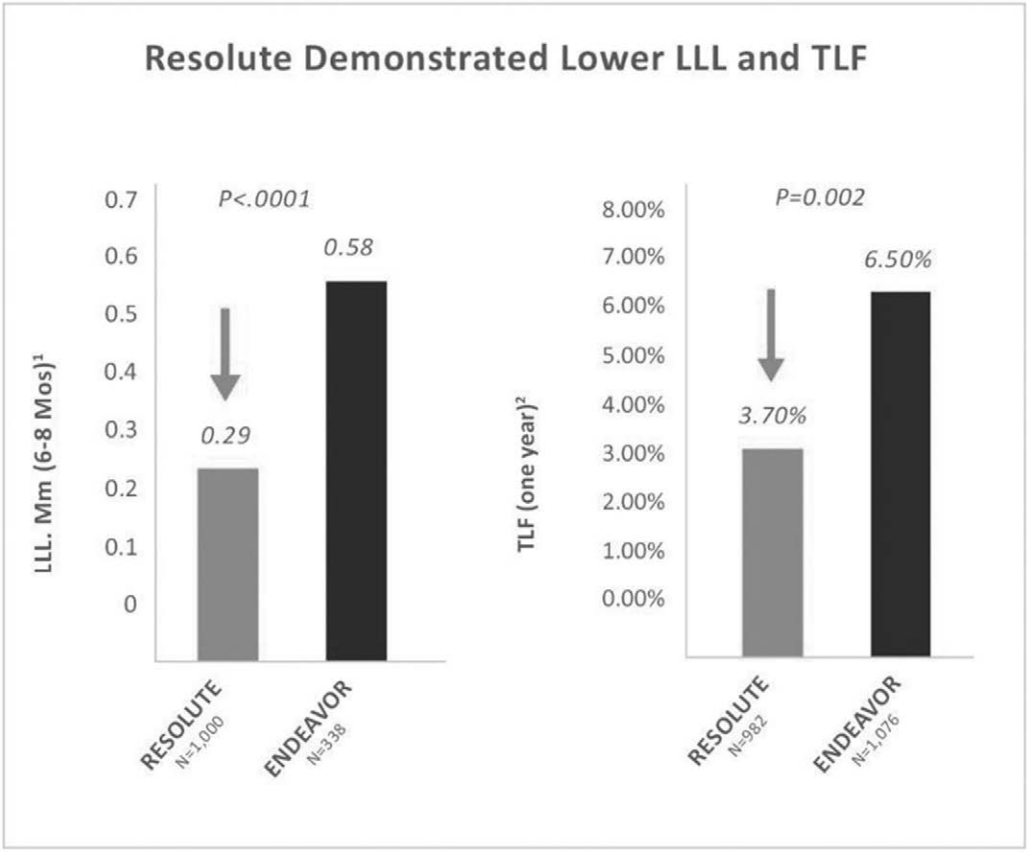


Source: Xinlin Zhang, et. al. PLOS ONE 2014 May 20;9(5):e97934.

Definitions: Adj-OS = adjusted observational study; Cl = confidence interval; No. = number of the studies; Non-adj OS = non-adjusted observational study; PES = paclitaxel-eluting stents; RCT = randomized controlled trial; RR = relative risk; SES = sirolimus-eluting stent; TLR = target lesion revascularization

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





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

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

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

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

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

- *The Use of Paclitaxel* — Despite the inferior performance observed in DES, most of the drug-coated balloons in use or in development globally deliver paclitaxel. The primary reason paclitaxel is used on drug-coated balloon technology is that paclitaxel has shown to be an easier pharmaceutical agent for balloon-based delivery due to fast tissue absorption and long tissue retention. On the contrary, delivery of 'limus agents has proven to be difficult based on two key reasons: (i) slow tissue absorption making it difficult to transfer the drug and ensure desired tissue absorption; and (ii) short half-life (the time it takes for the amount of drug present to be reduced by 50%) makes it challenging to ensure that therapeutic concentration of the drug is present for the critical, four-week healing period.

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

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

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

- *Balloon Surface Coating* — Drug-coated balloons utilize surface coatings for drug delivery which carry inherent limitations such as: (1) drug dosing that is constrained to what can incorporated in a balloon surface coating, (2) risk of emboli (e.g., a blood clot or other blockage) from large coating particulates that may cause downstream ischemia (an inadequate blood supply) in non-target tissues, and (3) significant drug loss during navigation of the balloon to the target lesion location in the artery. Published quantitative analysis of various drug-coated balloons showed a substantial number of large particles (>300μm). Large particles have the potential to occlude microvessels downstream following balloon inflation.

- In addition, third-party clinical data demonstrated that 50 – 80% of drug was washed or scraped off during transit to the target lesion prior to balloon inflation. Concerns of drug loss in transit and risk of particulates have prompted existing drug-coated balloon manufacturers to recommend balloon inflation within 30 seconds of balloon insertion into the patient, making it challenging for physicians to reach target lesions and ensure proper placement in such a short period of time, particularly in difficult coronary and peripheral lesions such ISR, small vessel disease, and below-the-knee disease.

Despite the limitations of paclitaxel-based DCBs, they are now widely used globally for the treatment of coronary ISR, coronary SV disease and other coronary indications. EU clinical guidelines recommend the use of DCBs for the treatment of coronary ISR based on clinical evidence. On March 1, 2024, Boston Scientific Corporation ("BSC") announced FDA approval for its AGENT™ paclitaxel-coated balloon for the treatment of coronary ISR. BSC launched the AGENT DCB commercially in the US in late 2024 and has reported rapid commercial uptake since launch. We believe the AGENT DCB is currently becoming the new standard of care for coronary ISR in the US.

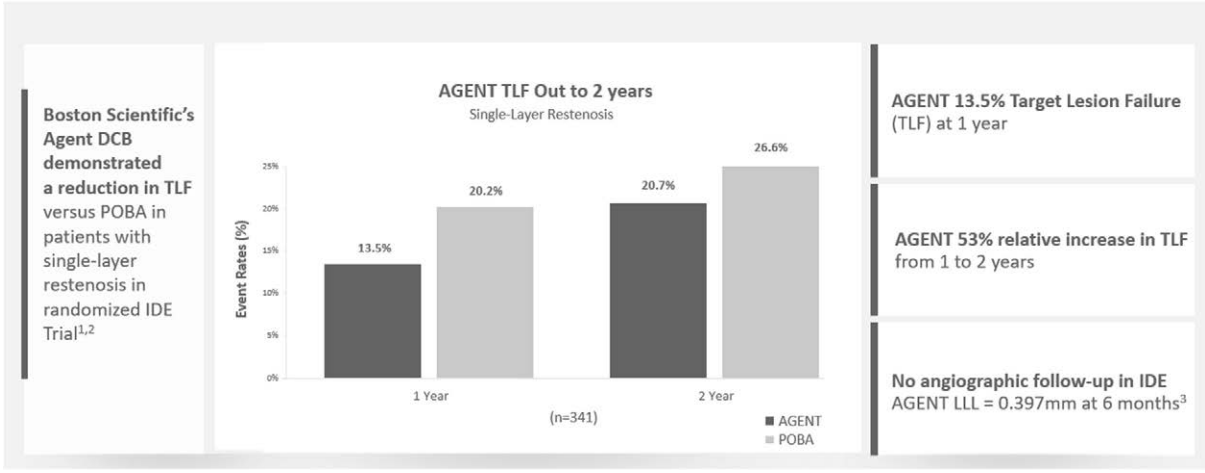
BSC has reported 2-year follow-up results from its US IDE study comparing the AGENT DCB to plain balloon angioplasty for the treatment of coronary ISR. These results showed statistical superiority for AGENT over plain balloon angioplasty with respect to the occurrence of TLF, the primary endpoint for the study. However, we believe the 17.9% reported rate of overall TLF at 1 year follow up is still high and creates a need and an opportunity for a differentiated, sirolimus-based product like Virtue SAB to demonstrate superior results and improve this standard of care. In the subgroup of patients that had single-layer ISR, AGENT DCB showed a TLF rate of 13.5% at 1 year follow up. This TLF result worsened by over 53% to 20.7% at 2-year follow-up.

At TCT 2025, Cordis reported preliminary results from its IDE study called SELUTION4ISR comparing the performance of its Selution SLR™ sirolimus-coated balloon to a "standard of care" control group including DES and plain old balloon angioplasty ("POBA") for the treatment of coronary ISR. While the Selution DCB achieved statistical non-inferiority to the control group, its results were numerically inferior.

Further, while 'limus-based DES consistently outperformed paclitaxel DES as described above, Selution DCB's 13.2% TLF rate in single-layer ISR were equivalent to the AGENT DCB results. The SELUTION4ISR and AGENT studies involved significantly different rates of double-layer stent ISR, making comparisons of overall performance difficult.

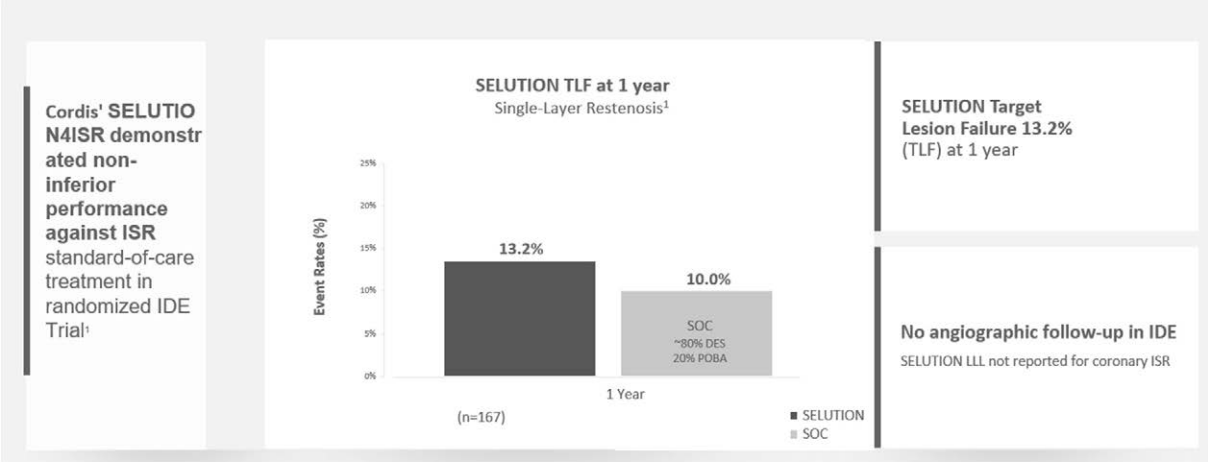
Overall, we believe Virtue SAB's performance in the SABRE study described below, particularly in the single-layer ISR per protocol population, reflects a promising opportunity for Virtue SAB in coronary artery treatment. However, please note that the AGENT study, the SELUTION4ISR study and the SABRE study are three separate studies conducted at different times and are not head-to-head comparisons of these therapies. Thus, the results of these studies may not be comparable.

AGENT IDE Trial Results Show Clear Opportunity for Virtue SAB



[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]Boston Scientific AGENT DCB Brochure 2017.
Definitions: Plain old balloon angioplasty (POBA), Standard of care (SOC), late lumen loss (LLL)

SELUTION4ISR IDE Trial Results Support Opportunity for Virtue SAB



[1]Cutlip et al. SELUTION4ISR Clinical Trial TCT 2025.

Targeted Unmet Needs and Market Opportunity for Virtue SAB

We believe significant unmet needs remain in certain artery disease indications where treatment options are limited or fail to adequately improve patient outcomes, including ISR, SV, high bleeding risk patients undergoing percutaneous revascularization and BTK. We estimate these indications currently represent a total addressable global market opportunity of approximately 5.0 million treatable artery disease lesions. Further, based on estimated regional average selling prices, we believe the current aggregate annual global market opportunity for Virtue SAB is at least $10 billion. The bullets below outline key potential market opportunities, including their relative size and scope, for Virtue SAB.

- *Coronary ISR:* The majority of coronary artery interventional procedures involve the placement of a permanent stent at the site of stenotic lesion. According to the National Cardiovascular Data Registry, restenosis within a stent occurs in 5 – 10% of stented patients during the first year and continues at a rate of up to 3% per year thereafter, resulting in what we currently estimate to be an annual addressable global market of nearly 347,000 lesions that may require treatment. Until recently, the only device treatments approved by the FDA specifically for use in coronary ISR lesions were balloon angioplasty and intravascular radiation therapy known as brachytherapy. However, brachytherapy is considered a last resort treatment due to expense, limited availability, and long-term requirement for dual antiplatelet therapy, and hence represents a small proportion of ISR procedures, while traditional balloon angioplasty has poor outcomes with high retreatment rates. Although DES are not approved for ISR, it is commonly used off-label despite the problems associated with multiple stent layers within the lumen of the vessel along with other limitations. Despite the limitations of paclitaxel-based DCBs, they are now widely used in the EU and Japan for the treatment of coronary ISR, coronary SV disease and other coronary indications. EU clinical guidelines recommend the use of DCBs for the treatment of coronary ISR based on clinical evidence. We estimate that potentially more than 30% of coronary interventions in the EU and Japan utilize a paclitaxel DCB. On March 1, 2024, BSC announced FDA approval for its AGENT™ paclitaxel-coated balloon for the treatment of coronary ISR following preliminary results from its US pivotal study showing statistical superiority for AGENT over plain balloon angioplasty with respect to the occurrence of TLF. We believe the 17.9% reported rate of overall TLF is still high and creates a need and an opportunity for a differentiated, sirolimus-based product like Virtue SAB.
- *De Novo Coronary Small Vessels (<=2.5 mm):* DES are difficult to position in vessels measuring less than or equal to 2.5 mm in diameter and may reduce already limited luminal area thereby impacting blood flow. We estimate, based on published data relating to specific country-wide lesion incidences, that there are approximately 1,500,000 patients with lesions in small diameter vessels that may require treatment worldwide.
- *De Novo Large Vessel (>2.5 mm):* Percutaneous coronary intervention ("PCI"), with placement of DES requires prolonged (greater than six months) treatment with dual antiplatelet therapy ("DAPT"), which is intended to prevent stent thrombosis or the development of blood clots on or around the metal struts of a stent. Stent thrombosis can lead to major adverse events such as heart attacks and death. We estimate, based on published data relating to specific country-wide lesion incidences, that patients with vessel diameter greater than 2.75 mm currently have an estimated 1,850,000 treatable lesions worldwide.
- *Below-the-Knee Lesions:* BTK disease is a form of PAD and is a primary cause of critical limb ischemia or lack of sufficient blood flow to the legs and feet. This may lead to amputation and increased risk of death. Diagnosis and treatment of BTK disease is highly fragmented with patients being diagnosed by internists, podiatrists as well as interventionalists. The Rutherford score is often used to classify patients with peripheral artery disease with 0 being asymptomatic and 6 being severe ischemic ulcers or gangrene. The patients with Rutherford score of 3 – 5 are most likely to benefit from an effective interventional BTK treatment. We estimate there are currently 1,242,000 treatable BTK lesions worldwide. Available endovascular treatment options are limited and often provide limited benefit. Balloon angioplasty has generally poor outcomes with high restenosis rates that require frequent retreatment for these lesions. DES and bare metal stents are used off-label to treat BTK lesions but suffer from strut fractures and kinking due to high torsion and potential for a crush injury in arterial lesions that are located between the knee and ankle. Disappointingly, BTK trials with paclitaxel-coated balloons to date have shown limited improvement over plain balloons as well as, in some cases, increased risk of amputation. While the cause of increased amputation risk has not been attributed to a specific factor, we believe this may be due to drug toxicity and the impact of flakes and large particulates from the balloon coating itself causing blockage in downstream capillaries or the cytotoxic effect of paclitaxel in these downstream locations.

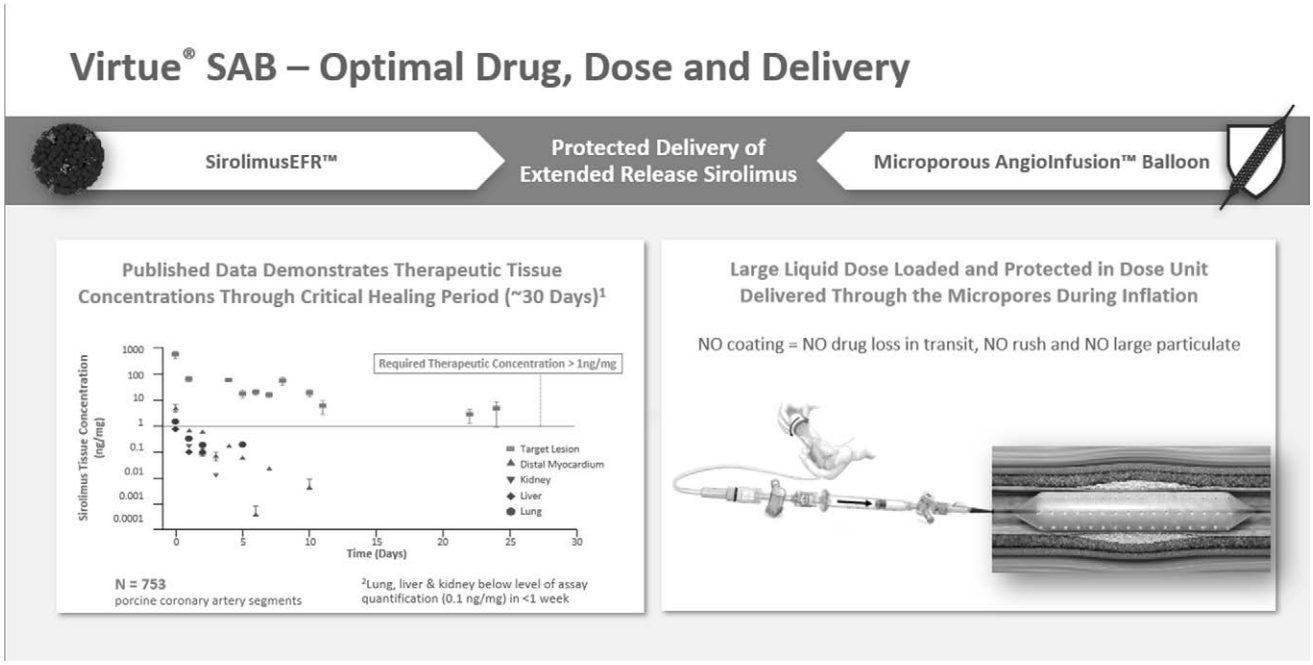
The above estimates are based on, among other factors, our engagement with an established market research firm to conduct market analysis of the Virtue SAB global opportunity. This third party employed primary and secondary data gathering and analysis methods. Primary analysis involved multiple Q&A calls with industry-leading key opinion leaders to help assess the addressable patient population and the most addressable patient segments. Secondary data analysis was conducted by mining numerous subscription-based market databases, Medicare data and published literature. After gathering initial disease prevalence data, both we and the third party spent extensive time collaborating on further delineating potential procedure volumes for coronary ISR, coronary SV disease, and BTK peripheral disease that can be addressed by Virtue SAB, taking into consideration patient treatment pathways, anticipated product benefits, competitive landscape and reimbursement. The market size calculations accounted for patients with high bleeding risk, which overlaps with all three target indications, and we believe will be an important driver of adoption. Our above estimate of 5.0 million treatable artery disease lesions is based on third-party data, combined with our knowledge of market dynamics and anticipated product differentiation.

Average selling price estimates were calculated by country or region based on existing competitive device prices, as well as estimated future pricing for Virtue SAB and future competitive devices. Reimbursement policies and coverage determinations for medical technologies are subject to evolving regulatory and market dynamics. The recent FDA approval and commercialization of BSC's AGENT may establish a clearer reimbursement pathway for DCBs, potentially benefiting our future market access strategy. As payors define coverage policies, coding, and payment rates for AGENT, we may benefit from an established precedent and streamline our engagement with Medicare, Medicaid, and private insurers, facilitating broader and more predictable coverage upon regulatory approval. Additionally, the adoption of a reimbursement framework for AGENT may expedite decision-making among payors, potentially leading to more favorable reimbursement terms for similar technologies, like Virtue SAB. While the evolving landscape presents opportunities, reimbursement determinations remain subject to various factors, including clinical differentiation, cost-effectiveness assessments, and provider adoption. We will continue to monitor and engage with key stakeholders to ensure alignment with emerging reimbursement policies that could enhance market access for Virtue SAB.

Impact Potential of Virtue SAB

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

- Delivering sirolimus without the need for a permanent implant or balloon coating;
- Protecting drug during transit to treatment site, preventing drug loss and reducing potential for downstream ischemia from large particulates;
- Performing angioplasty using standard catheter techniques without navigation and deployment time constraints; and
- Delivering the intended dose of sirolimus consistently



[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

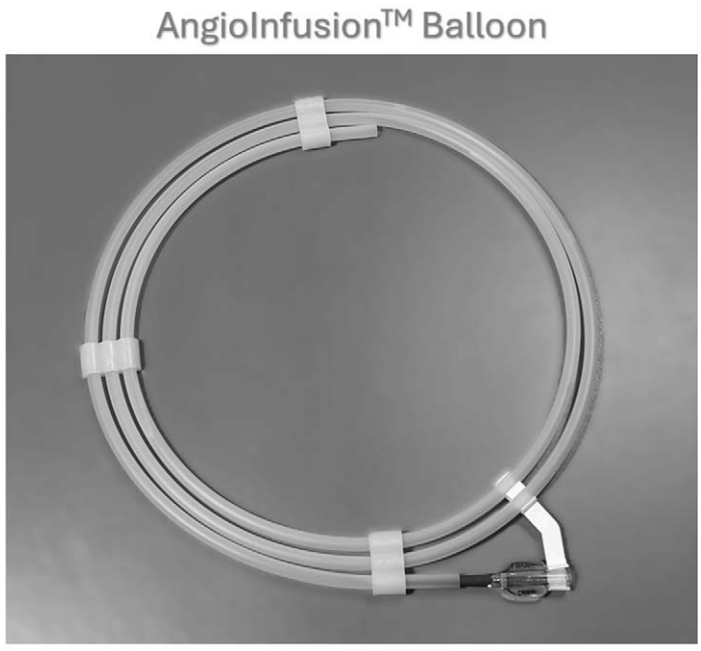
The differentiated design of Virtue SAB was made possible by combining two key technologies:

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

Virtue SAB System Components and Deployment

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

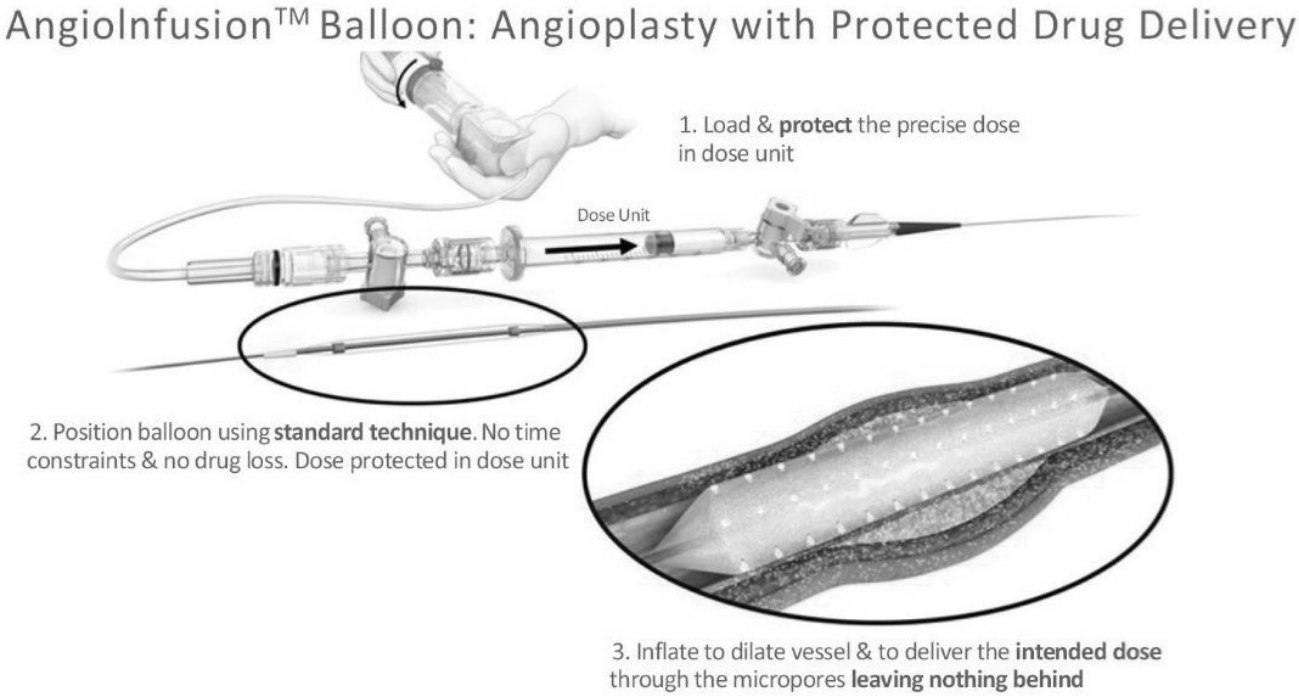
- *AngioInfusion Balloon Package:* This package includes the AngioInfusion Balloon along with a Compliance Card explaining the pressures needed for full balloon expansion, a Dose Chart which defines the dose of SirolimusEFR to be utilized for each balloon size, and the proposed Instructions for Use ("IFU") for the system. To accommodate various vessel sizes and lesion diameters, we expect end users would need to stock an array of AngioInfusion Balloon sizes. The AngioInfusion Package is expected to be stored at room temperature with a target shelf-life of two years at commercial launch (shelf-life independent of SirolimusEFR Package), if approved.



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

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

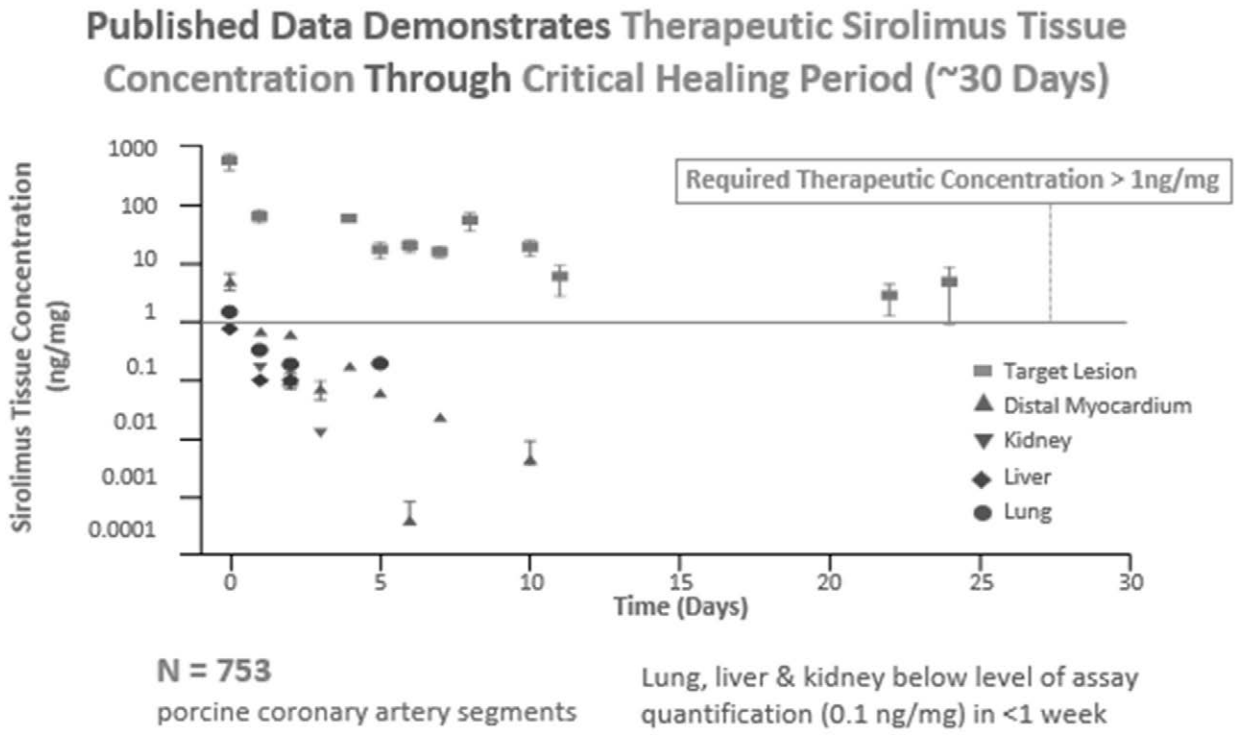
1. *Reconstitute the formulation and set dose*
    - SirolimusEFR is designed to be provided as a lyophilized (freeze-dried) powder that is reconstituted using provided components prior to the angioplasty procedure. Each balloon size is designed to deliver a specific volume of SirolimusEFR. Based on the balloon size selected, the required dose volume of the reconstituted liquid formulation is loaded into the Dose Unit. The SirolimusEFR-loaded Dose Unit is connected to the AngioInfusion Balloon catheter.
2. *Prime the catheter*
    - The AngioInfusion Balloon is a semi-compliant microporous balloon. After the Dose Unit is connected, the AngioInfusion catheter is primed with the formulation using a standard endoflator device used in all catheterization labs prior to insertion into the patient and navigation to a target lesion. The dose remains protected in the catheter and the Dose Unit.
3. *Position AngioInfusion Balloon and inflate*
    - Similar to standard angioplasty, a guidewire and guide catheter are placed, and the balloon is positioned at the lesion using radiopaque marker bands. When satisfied with device positioning, the physician inflates the AngioInfusion Balloon to perform standard high-pressure angioplasty. The intended dose of SirolimusEFR is delivered simultaneously through the micropores to the target lesion.



Preclinical Data

We have conducted extensive preclinical testing of Virtue SAB and its key enabling technologies (SirolimusEFR and the AngioInfusion Balloon), including feasibility work as well as Good Laboratory Practice ("GLP") studies in support of regulatory filings and approvals. This work includes a variety of benchtop as well as small and large animal models. Large animal studies have been conducted in a porcine animal model, a widely used model for testing interventional cardiovascular devices. A particularly important series of preclinical studies involving 130 pigs and over 750 distinct artery treatment sites showed that Virtue SAB provided extended focal release of therapeutic levels of sirolimus through the critical healing period of approximately four weeks. The data from these preclinical studies was published in the peer-reviewed EuroIntervention Journal in 2016 and showed that Virtue SAB successfully delivered and enabled long-term focal delivery at the treatment site of a therapeutic sirolimus dose (above the 1ng of drug per mg of tissue). This therapeutic dose level has been clinically proven using DES to be safe and efficacious at reducing restenosis during the critical healing period of approximately 30 days post-procedure. These preclinical studies also showed very low systemic concentrations in cardiac tissue as well as critical organs, such as lungs, liver and kidneys, and did not show any adverse local or systemic effects.

In March 2024, we shared preclinical pharmacokinetic ("PK") data demonstrating that Sostenocel™, the proprietary polymer system enabling Virtue SAB's SirolimusEFR, was shown to be eliminated in SirolimusEFR-treated stented arteries without detectable degradation. In other polymer-based delivery systems, degradation prior to elimination is associated with adverse events, such as the development of localized tissue inflammation. Specifically, the presented PK data showed that Sostenocel was undetectable at 90 days in treated arteries and at 3 days in all non-target tissues, and the molecular weight of Sostenocel remained unchanged prior to elimination, showing no evidence of in-vivo degradation. This is achievable through the focal uptake extended release of Sostenocel technology.



Clinical Results

SABRE Study Results

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

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

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

Revised Per-Protocol Population

A revised per-protocol population was determined based on analysis of procedural data by an independent core lab. This analysis identified 14 cases out of the 50 patients treated in the SABRE study that represented serious violations of the established inclusion and exclusion criteria of the protocol for the study. Eight cases were excluded due to excessive proximity to the aorta or major side branches. Three cases were excluded due to treatment of lesions that were longer than the available Virtue SAB devices were designed to treat or because there were multiple lesions in the vessel where there was a target lesion. Finally, three cases were excluded due to double-layer stent ISR where Virtue SAB was used to treat to previously stented restenosis (*i.e.*, the lesion already had two overlapping treatment stents). The remaining 36 patients with single-layer ISR are referred to herein as the revised per-protocol, population.

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

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

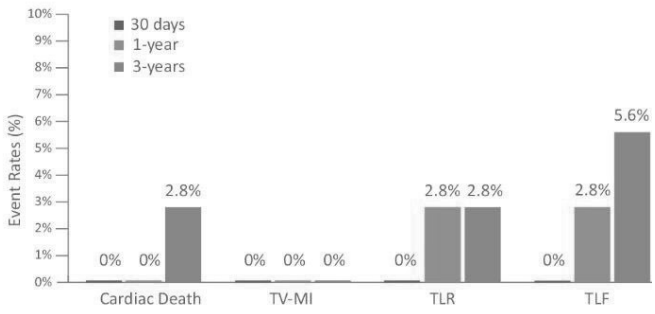
A total of 37 SAEs in 25 patients were non-cardiac-related, none of them were adjudicated as "highly probable," "probable," or "possible" related to either the device treatment procedure or the investigational device. A total of eleven patients had both cardiac- and non-cardiac-related SAEs.

Preliminary Efficacy Results Showed Low 0.12mm Late Loss

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

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

Preliminarily Demonstrated Safety with Low Event Rates Out to 3 Years[1]



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

Intent to Treat Population

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

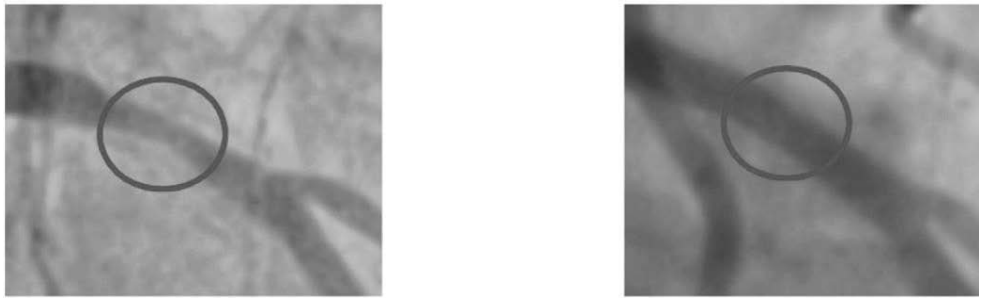
Two-year and three-year clinical follow-up results from the SABRE study were presented at the TCT conference in 2017 and 2018, respectively. We believe the angiographic and clinical results of the SABRE trial are encouraging and provide the basis for it to conduct the upcoming Virtue ISR-US pivotal clinical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

Angiograms of Virtue SAB in Patients

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

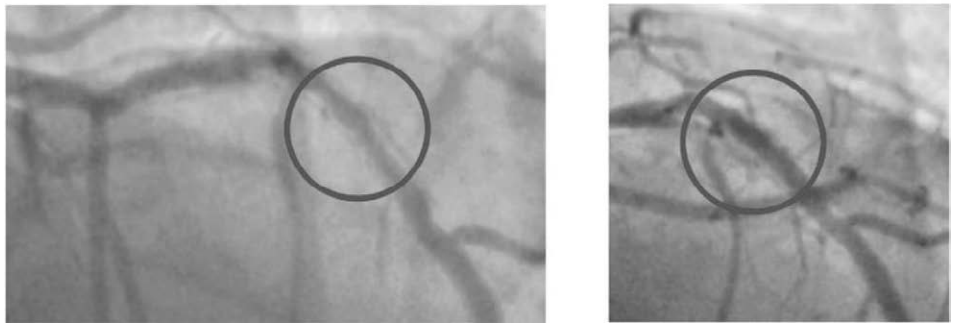
Patient 1 (06-03): Patient presented with an 11.54 mm lesion in the mid-left circumflex artery. Lesion was previously treated with a BMS. The patient's lesion was pre-dilated (a standard practice in drug-eluting balloon procedures) with a non-compliant balloon (a balloon that expands to one specific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

Baseline Angiogram **6 Month Follow-Up**



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

Baseline Angiogram **6 Month Follow-Up**



The Virtue Trial, FDA Regulatory Status & Breakthrough Device

On April 29, 2025, we announced IDE approval from the FDA for the Virtue Trial, a pivotal trial to be conducted at up to 75 sites in the U.S. that is expected to randomize approximately 740 patients 1:1 to either treatment with Virtue SAB or Boston Scientific Corporation's AGENTTM paclitaxel-coated balloon (currently the only drug-coated balloon approved in the U.S. for a coronary indication) with a primary efficacy and safety endpoint of statistical non-inferiority of target lesion failure ("TLF") at 12 months post index treatment.

On October 27, 2025, we announced that we had initiated enrollment of patients for the Virtue Trial. We currently estimate completion of enrollment of the Virtue Trial in mid-2027; however, there is no assurance that our current operating plan will be achieved. To execute and support clinical activities for the Virtue Trial we plan to use (1) full-time employees as well as full- and part-time consultants to directly manage clinical studies and supervise external providers; (2) an external contact research organization ("CRO"), that serves as the authorized and legal representative of the study sponsor, submits study protocol for approval by clinical site review boards and ethics committees, and reports adverse events; and (3) an independent core lab and independent imaging analysis lab.

We currently anticipate using the Virtue Trial results to support regulatory approval for Virtue SAB for the treatment of coronary ISR. The FDA previously confirmed that Virtue SAB will be regulated as a combination product candidate, with the FDA's Center for Devices and Radiological Health as the lead review center of a marketing application. In addition, Virtue SAB has been granted Breakthrough Device designation in:

- *Coronary ISR* — for the balloon dilatation of the stenotic portion (up to 26 mm in length) of a stented coronary artery that is 2.25 mm to 4.0 mm in diameter, for the purpose of improving lumen diameter;
- *Coronary SV* — for the balloon dilation of the de novo stenotic portion (up to 26 mm in lesion length) of a native coronary artery of 2.0 mm to 2.5 mm in diameter (small coronary arteries), for the purpose of improving lumen diameter; and
- *Peripheral BTK* — for the balloon dilatation of the stenotic portion (up to 18 cm in length) of an infrapopliteal artery (P-3 segment or distal, below the knee, with reference vessel diameter 2.25 – 4.0 mm), for the purpose of improving lumen diameter.

SirolimusEFR — Additional Interventional Therapies Product Candidates and Development Initiatives

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

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

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

We believe we have a future opportunity to develop additional therapies using our proprietary SirolimusEFR to potentially treat focal inflammation outside of coronary and peripheral vascular indications. Further, we are currently working on all chemistry, manufacturing and controls ("CMC") testing for our IDE submission for the combination product Virtue SAB that includes populating a drug master file ("DMF"). We believe this DMF will be helpful in supporting additional vascular regulatory indications for Virtue SAB as well as future potential non-vascular indications for SirolimusEFR, with or without our microporous angioinfusion balloon technology. Depending on the indication, we may be able to leverage some of the biocompatibility and CMC data in the DMF, while providing additional data depending on the indication selected. Leveraging CMC data in the DMF, as well as other preclinical, clinical and device testing work related to Virtue SAB, may allow us to advance development of additional SirolimusEFR-based product candidates at an accelerated pace and at reduced cost, although no assurances can be given that development will proceed faster or at lower expense than otherwise expected.

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

Our Future Growth Strategy

Our growth strategy is primarily focused on the execution of key development initiatives and partnership opportunities within our existing product pipeline, with the objective to advance these product candidates to key value inflection points and to form strategic partnerships for commercial value realization. This includes advancing clinical study activities for our flagship product candidates, as well as moving earlier stage product candidates further into clinical development. In the future, we may look to potentially expand our pipeline through collaborations or spinouts with corporate partners, targeted acquisitions that are made in parallel to forming strategic collaborations, royalty-based research and development partnerships, as well as highly selective organic development or intellectual property licensing.

We carefully screen new opportunities utilizing our focused innovation selection criteria to ensure a fit with our partnership-enabled business model.

- ***Target mature therapeutic device markets with significant unmet needs.*** Product innovations that address known unmet clinical and procedural needs in established medical markets with entrenched leaders and slowed product innovation.

- ***Provide high-impact, procedure-based solutions with rapid adoption potential.*** Transformative technology solutions with the potential to improve clinical outcomes and lower costs of care while fitting existing treatment paradigms and having well-defined development pathways.

- ***Offer strategic and financial benefits to a commercial partner and us.*** Innovative technologies that are protected by strong intellectual property offer distinct advantages that can be leveraged to disrupt competitive dynamics and have the potential to provide attractive profit margins to support favorable partnership economics.

Our Team and Innovation History

We are led by a highly accomplished, multidisciplinary management team with extensive experience and strong expertise in all phases of therapeutic product development. Our senior management team, including the vice president-level and above, has over 300 years of combined experience, with an average tenure of 25 plus years in the development and commercialization of procedure-based innovations for major clinical indications. Our team's expertise includes clinical need and market analysis, product design and intellectual property prosecution, clinical and regulatory execution, as well as supply chain and quality system development. Members of our senior management team have been personally involved in the development and regulatory approval or clearance of over 100 products and have helped author over 600 patent applications. Our executive team is guided by a seasoned and highly accomplished board of directors with knowledge and experience in the healthcare industry, including medical devices, biotechnology and clinical medicine, as well as business operations, strategy, finance and capital markets. Further, our product development efforts are supported by world-renowned medical advisors who are physicians and scientists recognized for their knowledge of specific disease states and treatment options available, as well as their ability to quickly assess new technologies for clinical feasibility and likelihood of adoption.

All the product candidates in our pipeline were conceived and developed by our management team and employees through predecessor companies founded by a medical device accelerator, Accelerated Technologies, Inc. ("ATI"). ATI was originally founded in 2000 and employed active collaboration with industry-leading physicians to identify and purpose-build transformational therapeutic devices. Our founders and senior executives, Mr. David Hochman, our Chief Executive Officer, and Mr. Darren Sherman, our President and Chief Operating Officer, joined ATI in 2006 and 2008, respectively. Prior to their joining, ATI was associated with the development of approved devices such as transcatheter aortic valve replacement (Percutaneous Valve Technologies, Inc., which was acquired by Edwards Lifesciences Corp. in 2003) and catheter-based temporary ventricular support (Impella CardioSystems AG, which was acquired by ABIOMED, Inc. in 2005). Mr. Hochman and Mr. Sherman assumed control of ATI in 2009 and proceeded to found new companies that developed Virtue SAB (Caliber Therapeutics), AVIM Therapy (BackBeat Medical), and the FreeHold Duo and Trio Retractors (FreeHold Surgical). Orchestra BioMed, Inc.'s business was formed in May 2018 upon the merger of these three entities and a concurrent recapitalization. ATI was subsequently acquired by Orchestra BioMed, Inc. in December 2019.

Our Strategic Holdings

We own outright or maintain ownership of minority equity interests, convertible debt and/or royalty-stream interests in additional therapeutic device assets currently undergoing early-stage commercialization and further product development that we believe have growth and value appreciation potential. Our objective is to create and realize additional stockholder value through ownership in innovative therapeutic product solutions in core, adjacent and synergistic medical segments. Our strategic holdings include:

- ***FreeHold Surgical*** — we own 100% of FreeHold Surgical, LLC, which has developed and commercialized on a pilot basis in the U.S. patented single-use FreeHold Hands-Free Intracorporeal Retractions ("FreeHold Devices") designed to help reduce required incisions and enhance laparoscopic and robotic procedures. FreeHold Trio and Duo hands-free intracorporeal retractors are regulated as Class I medical devices by the FDA and are generally indicated for internal organ or tissue retraction during minimally invasive procedures. We believe FreeHold devices are the only fully and continuously adjustable, completely intracorporeal devices specifically designed to address limitations of the available retraction methods. These devices are designed to enable a variety of advanced robotic and laparoscopic surgical procedures for the treatment of obesity, GI disorders and other indications. Their versatile design makes retractors appropriate for a broad range of minimally invasive procedures, including bariatric and foregut surgeries, nephrectomies, colectomies, cholecystectomies, paraaortic node dissections, hysterectomies, and other procedures. We believe FreeHold devices are designed to offer several potential advantages over existing retraction options:

- Improve Patient Care
  - No additional incisions required as they are deployed through same access incisions as used in standard procedures;
  - Minimize complications from suboptimal visualization and additional incisions; and
  - Avoid trauma associated with the use of Nathanson-type retractors
- Enable Full Surgeon Autonomy
  - Surgeon controls positioning and adjustment of retractor;
  - Once positioned, surgeon has full use of both hands to perform surgery; and
  - No coordination with circulator required
- Optimize Visualization
  - Easily adjustable throughout the procedure for sustained visibility; and
  - Low profile design minimizes procedural clutter and collisions

Targeted Commercialization — We estimate over 20,000 procedures using FreeHold devices have been performed in the United States to date, primarily in bariatric (obesity) and foregut (GI, metabolic) surgeries with some initial experience in paraaortic node dissections (gynecologic oncology), nephrectomies (kidney removal) and cholecystectomies (gallbladder removal). FreeHold's targeted commercial development program involves only two dedicated sales representatives targeting hospitals in the United States to demonstrate clinical utility and commercial demand for FreeHold Devices.

Strategic Potential — We believe FreeHold devices have been optimized for strategic partnership because they are highly differentiated, enabling products that fit into the current treatment paradigms, are easy to use with a relatively short learning curve and have sufficiently high profit margins that provide potential for partnering to enable a revenue sharing arrangement.

Formation and Conversion to a Limited Liability Company — In May 2018, Orchestra BioMed, Inc. completed its acquisition of FreeHold Surgical, Inc., a Delaware corporation that has, among other things, the rights to our FreeHold Devices. FreeHold Surgical, Inc. was incorporated in Delaware in May 2010 and began development of its hands-free, intracorporeal retractors for minimally invasive surgery in 2012. In December 2019, Orchestra BioMed, Inc. converted FreeHold Surgical, Inc., a Delaware corporation, to FreeHold Surgical, LLC, a Delaware limited liability company. References in this annual report to FreeHold refer to FreeHold Surgical, Inc. prior to its conversion to a limited liability company and to FreeHold Surgical, LLC after its conversion to a limited liability company, as applicable.

- ***Motus GI —*** We own 100% of Motus GI Medical Technologies Ltd., an Israeli corporation ("Motus GI Technologies") and Motus GI, LLC, a Delaware limited liability company ("Motus Delaware" and, collectively, with Motus GI Technologies, the "Motus Entities"), which has developed the Pure-Vu® System, a medical device that has been approved by the FDA to facilitate the cleansing of a poorly prepared gastrointestinal tract during colonoscopy and to help facilitate upper gastrointestinal (GI) endoscopy procedures. The Pure-Vu® System is also CE marked in the EU for use in colonoscopy. The Pure-Vu® System integrates with standard and slim colonoscopes, as well as gastroscopes, to improve visualization during colonoscopy and upper GI procedures while preserving established procedural workflow and techniques. Through irrigation and evacuation of debris, the Pure-Vu® System is designed to provide better-quality exams as well as enable the completion of exams that otherwise could not be completed due to obstructed visualization. Challenges exist for inpatient colonoscopy and endoscopy, particularly for patients who are elderly, with comorbidities, or active bleeds, where the ability to visualize, diagnose and treat is often compromised due to debris, including fecal matter, blood, or blood clots. We believe this is especially true in high acuity, high risk patients, like those experiencing GI bleeding where the existence of blood and blood clots can impair a physician's view and removing them can be critical in allowing a physician the ability to identify and treat the source of bleeding on a timely basis.

Market Opportunity & Commercial Experience — We estimate that there are approximately 1.5 million inpatient colonoscopy procedures that were performed in the U.S. and approximately 4.8 million worldwide annually, based on our analysis of market data and projections from iData Research Inc. Upper GI bleeds occurred in the U.S. at a rate of approximately 400,000 cases per year in 2019, according to iData Research Inc. The Pure-Vu System has been assigned an ICD-10 reimbursement classification code in the U.S., and we believe the clinical and health economic benefits offered by the Pure-Vu System make its use financially supportable under existing reimbursement payments for inpatient procedures. The Pure-Vu System does not currently have unique or dedicated reimbursement codes for specific additional reimbursement with any private or governmental third-party payors in any other country or for any other use; however, we may pursue reimbursement activities in the future. The Pure-Vu® System is designed to reduce the time required to complete colonoscopy procedures, which may make it attractive to closed healthcare systems, such as the Veterans Affairs hospital system ("VA"), that are insured by their constituents and bear the cost burden of lengthened hospital stays due to colonoscopy preparation. The Pure-Vu System is designed to reduce hospital stays through more efficient colonoscopy procedures, potentially saving money and expediting care. Additionally, VA patients may have increased complications with colonoscopy preparation due to the co-morbidities that veterans can experience. Thus, the potential clinical benefit to VA patients of the Pure-Vu product may be important as well, as the system is designed to remove debris and enhance the field of view during a colonoscopy procedure in the event the pre-procedure preparation was not optimal. The Pure-Vu System is currently in pilot commercial use in 8 hospitals in the U.S., including two VA hospitals. We anticipate increasing Pure-Vu System pilot use to approximately 20 U.S. hospitals in 2025, with a particular focus on the VA where we anticipate conducting structured clinical evaluations aimed at supporting broader VA system adoption. We also expect to obtain CE Mark approval for the next generation of the system with both the upper and lower indication and introduce the system to a few select hospitals in the EU and Israel.

Strategic Potential — We believe use of the Pure-Vu® System has the potential to help achieve better clinical outcomes and lower costs for hospitals by safely and quickly improving visualization of the colon and upper GI tract, potentially enabling effective diagnosis and treatment without delay. In multiple clinical studies to date, involving the treatment of challenging inpatient and outpatient cases, the Pure-Vu® System has consistently helped achieve adequate bowel cleanliness rates greater than 95% for inpatients and outpatients following a reduced prep regimen. We also believe that the technology may be useful in the future as a tool to help reduce user dependency on conventional pre-procedural bowel prep regimens and enhance the treatment of acute upper GI bleeding. We believe the Pure-Vu System is potentially attractive for strategic partnership because it is a proprietary enabling technology that addresses significant unmet needs in a large established global market, its usage fits into current treatment paradigms and is easy enough to use with a relatively short learning curve, and its disposable component has sufficiently high profit margins that provide potential for partnering to enable a revenue sharing arrangement.

Acquisition of Motus Entities — In October 2024, we entered a Share and Membership Interest Purchase Agreement with the previously publicly traded company, Motus GI Holdings, Inc. and its lender, Kreos Capital VI, LP. to acquire the Motus Entities for the rights to the intellectual property of the Pure-Vu® System.

- ***Vivasure Medical —*** As of December 31, 2025, we owned a minority equity interest, representing approximately 10.9% in Vivasure Medical Limited ("Vivasure"), a Galway, Ireland-based company that develops advanced polymer implants and delivery systems, primarily focused on minimally invasive vessel closure in cardiology, interventional radiology and vascular surgery. On January 9, 2026, Haemonetics Corporation ("Haemonetics"), a U.S. medical device company, closed on an acquisition of Vivasure in which we expect to receive up to $21.0 million in cash proceeds. We can receive up to $10.7 million of proceeds in 2026 made up of a $4.7 million upfront, which was received on January 9, 2026, and approximately $6.0 million in a first milestone payment. The remainder of the proceeds may be received in future revenue earnouts based on the achievement of certain milestones in a period greater than one year.

Our Research and Development

We invest in research and development efforts that advance and expand our product pipeline. Our goals are to: (1) deliver on clinical, regulatory and commercial development objectives for Virtue SAB; (2) deliver on clinical, regulatory and commercial development objectives for AVIM Therapy set forth in collaboration with our strategic partner, Medtronic; and (3) further develop pipeline product candidates towards future partnerships with potential strategic partners. Our research and development expenses totaled $58.2 million for the year ended December 31, 2025 and $42.8 million for the year ended December 31, 2024.

We believe our ability to rapidly develop innovative product candidates is attributable to the dynamic product innovation process that we have implemented, the versatility and leveragability of our core technologies and our partnership-enabled business model that drives our innovation objectives and research and development process. We have recruited and retained engineers and scientists with significant experience in the development of medical devices. We have a pipeline of product candidates in various stages of development that are expected to provide additional strategic opportunities. Our research and development efforts are based at our facilities in New Hope, Pennsylvania and Fort Lauderdale, Florida.

Our Manufacturing and Supply

Bioelectronic Therapies (AVIM Therapy and CNT-HF)

Our wholly owned subsidiary, BackBeat Medical previously contracted with a business unit of Integer under an agreement (the "Integer Agreement") to develop and manufacture the Moderato device. The Moderato device consists of an IPG powered by a primary battery, a programming system integrated by a programmer interface, a telemetry wand and a software application capable of programming standard pacing functions as well as the different parameters of AVIM Therapy. All intellectual property that Integer developed for BackBeat Medical during the performance of the Integer Agreement, whether developed independently or jointly, and that resulted from or uses BackBeat Medical's technology or intellectual property are owned by BackBeat Medical. Under the Integer Agreement, Integer provided BackBeat Medical a perpetual, royalty-free, fully paid, assignable, world-wide, non-exclusive license for the device-incorporated Integer property, allowing the use of the incorporated Integer property only within BackBeat Medical's field of use (electrical therapies, particularly cardiac pacing for (i) treatment of HTN and (ii) rhythm management in patients that were implanted with a device for the treatment of HTN). We also utilize the services of external consultancy firms for quality and regulatory services related to Moderato devices to supplement its internal capabilities. As of the date of this filing, we do not anticipate receiving any new Moderato devices under the Integer Agreement.

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

In February 2023, we also contracted with MEDICO S.R.L. to develop a dual chamber pacemaker device that meets our specifications for running our cardiac neuromodulation therapies as well as standard pacing algorithms. This new device platform is designed to allow us to conduct CNT program studies for potential expanded indications and populations, including certain heart failure patients. Initial devices have been delivered, and we are actively engaging centers with a new protocol to conduct clinical evaluations which commenced in 2025.

Interventional Therapies (Virtue SAB, SirolimusEFR and Sostenocel)

Microporous AngioInfusion Balloon and other device components of Virtue SABs

Currently, we manage the supply chain, and these devices are manufactured by a selected group of third parties contracted by us. All of Virtue SAB's key suppliers and vendors carry the proper quality system certification and/or FDA approvals for the activity they are providing in support of the manufacturing, testing, storage and distribution of components, materials, services or final product.

SirolimusEFR

We have internal capabilities for small scale production (300 vials per run), lyophilization, and characterization testing for SirolimusEFR. Clinical and commercial production has been contracted through an established clinical manufacturing organization with large scale current Good Manufacturing Practice ("cGMP") production capabilities. We have scaled clinical production with an external manufacturing partner to achieve a capacity of approximately 3,000 vials per run with further scaling planned to reach planned commercial production capacity. Additional contract vendors provide polymer synthesis capabilities based on world-class polymer expertise in order to supply enabling components to the Sostenocel technology used to create SirolimusEFR. cGMP syntheses have been performed, with extensive analytical method, and quality control development complete. Synthesis of custom polymers has successfully achieved clinical scale with ongoing work to scale processes to commercial scale.

FreeHold Devices

We utilize an FDA-registered and ISO 13485-certified U.S.-based manufacturing partner to manufacture FreeHold Duo and FreeHold Trio intracorporeal retractors. Our manufacturing partner also provides warehousing and distribution of its products to qualified customers based on orders placed by customers to its FreeHold Surgical subsidiary. We have utilized the same manufacturing partner since the time of FDA product registration. Further, our manufacturing partner has achieved a greater than 99% on-time order delivery rate to our customers.

Motus Devices

We have established relationships with research facilities, contract manufacturing organizations, or CMOs, and our collaborators to manufacture and supply our product for our initial U.S. market development efforts targeting early adopter hospitals and selective closed systems like the Veterans Affairs hospital system. Currently, the workstation component of our Pure-Vu® System is manufactured by Sanmina Corporation at their facilities in Israel. The disposable portion of the Pure-Vu EVS is manufactured by Sterling Industries in their Michigan, U.S. facility. These manufacturing suppliers have extensive experience in medical devices and in dealing with regulatory bodies and other competent entities. These suppliers have ISO 13485 certified quality systems. We have an agreement in place with a third-party logistics provider in the U.S. who is ISO 13485 certified and specializes in medical devices and equipment. They provide warehousing, shipping and back-office support to meet our commercial needs with respect to our Pure-Vu® System.

Our Competition

The medical device industry is intensely competitive, subject to rapid change and significantly affected by new product introductions and other market activities of industry participants. We compete or plan to compete with developers, manufacturers and distributors of cardiovascular and other medical devices. Regarding Virtue SAB, our most notable competitors in the highly competitive interventional cardiology field include Boston Scientific Corporation, Medtronic plc, Becton Dickinson, Philips N.V., B. Braun, Abbott Laboratories, Cordis, Teleflex, Inc., Concept Medical, Inc., MicroPort, Eurocor Tech GmbH, iVascular, S.L.U., Biosensors International Group, Ltd., Balton, Invamed, Inc., and others. Regarding AVIM Therapy, our potential competitors in the field of cardiac rhythm management devices include Abbott Laboratories, Boston Scientific Corporation, BIOTRONIK, Inc., and MicroPort CRM and others.

Many of these competitors are large, well-capitalized companies with significantly greater market share and resources than we have. Consequently, they are able to spend more on product development, marketing, sales and other product initiatives than we can. We also compete with smaller medical device companies that have single products or a limited range of products. Some of these competitors have:

- significantly greater name recognition;
- broader or deeper relations with healthcare professionals, customers and third-party payors;
- more established distribution networks;
- additional lines of products and the ability to offer rebates or bundle products to offer greater discounts or other incentives to gain a competitive advantage;

- greater experience in conducting research and development, manufacturing, clinical studies, marketing and obtaining regulatory clearance, certification or approval for products; and
- greater financial and human resources for product development, sales and marketing and patent prosecution.

We believe that our proprietary AVIM Therapy, Virtue SAB and other pipeline technologies, our partnership-enabled business model, our strategic partnerships, such as the Medtronic Collaboration for AVIM Therapy and our organizational culture and strategy will be important factors in our future success. We compete primarily on the basis that our products are designed to improve outcomes, reduce complications and provide distinct commercial advantages that can be leveraged by us and our strategic partners. Our continued success depends on our, and in some cases, our strategic partners' ability to:

- develop innovative, proprietary products that can cost-effectively address significant clinical needs in a manner that is safe and effective for patients and easy to use for physicians;
- continue to innovate and develop scientifically advanced technology;
- forge risk and reward sharing partnerships with established commercial market leaders to help support product development and commercialization;
- obtain and maintain regulatory clearances, certifications or approvals;
- demonstrate efficacy in sponsored and third-party clinical studies;
- obtain and maintain adequate reimbursement for procedures using its products;
- apply technology to develop pipeline product candidates for additional clinical indications;
- attract and retain skilled research and development and sales personnel; and
- cost-effectively manufacture and successfully market and sell products.

Our Intellectual Property

Our success depends in part on our ability to obtain, maintain, protect and enforce our proprietary technology and intellectual property rights, and, in particular, our patent rights, as well as our ability to preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and other intellectual property rights of third parties. We rely on a combination of patent, trademark, trade secret, copyright and other intellectual property rights and take measures to protect the intellectual property rights that we consider important to our business.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term can be extended to recapture a portion of the United States Patent and Trademark Office's (the "USPTO") delay in processing the patent to issue as well as restore a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. We cannot be sure that our pending patent applications that we have filed or may file in the future will result in issued patents, and we can give no assurance that any patents that have issued or might issue in the future will protect our current or future products, will provide us with any competitive advantage, and will not be challenged, invalidated, or circumvented.

We also rely on trade secret know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary rights through a variety of methods, including confidentiality agreements with suppliers, consultants and others who may have access to our proprietary information and proprietary information and inventions agreements with our employees. However, trade secrets and proprietary information can be difficult to protect. While we take measures to protect and preserve our trade secrets and proprietary information, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our competitors may independently discover or develop the same trade secrets and proprietary information as us. To the extent that our suppliers, employees, consultants and others use intellectual property owned by others in their work for us, we may be subject to allegations of infringement and further disputes may arise as to the rights in related or resulting improvements, know-how and inventions.

Our success also depends in part on not infringing the intellectual property rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to intellectual property rights that we may require to develop or commercialize our future product candidates may have an adverse impact on the business. If third parties have prepared and filed patent applications in the United States prior to March 16, 2013 (the date when U.S. patent law changed from granting rights to the first-to-invent to the first-to-file) that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. For more information regarding the risks related to our intellectual property, please see the section titled *"Risk Factors — Risks Related to Our Intellectual Property."*

Trademarks

As of December 31, 2025, we have 8 trademarks that are approved in the United States: "Orchestra BioMed," "Moderato," "Virtue", "FreeHold Surgical," "FreeHold Duo," "FreeHold Trio," "Pure-Vu System," and "Motus GI." A further 10 applications for trademark registration are pending, covering "OBIO," "SirolimusEFR," "AngioInfusion," "Virtue Sirolimus AngioInfusion Balloon," "BackBeat Medical," "BackBeat CNT," "BackBeat Cardiac Neuromodulation Therapy," "Moderato Plus," "Sostenocel," and "MICRO-PREP." The trademark "Orchestra Biomed Inc." is approved in Japan (only). This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our right or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Material Patents

As of December 31, 2025, we owned 241 patents globally, of which 82 were issued U.S. patents and 159 were patents outside of the United States.

Our issued patents expire between March 2026 and April 2041. Despite the near-term expiration of certain of our material patents, we believe that our other patents, as well as our trade secrets and continuing technological know-how, provide us with sufficient intellectual property protection to develop our product candidates and protect our intellectual property.

Below is a more specific overview of our intellectual property as it relates to our pipeline programs by modality:

Bioelectronic Therapies (AVIM Therapy and CNT-HF)

AVIM Therapy and CNT-HF are protected by an intellectual property portfolio which currently includes 44 issued U.S. patents and 94 issued patents in countries outside of the United States encompassing devices, algorithms, and methods. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2026 and 2041, without taking potential patent term extensions or adjustments into account. Additional patent applications are filed on a regular basis. BackBeat issued patents are divided between CNT and CNT-HF as follows: 40 issued U.S. patents and 80 issued patents in countries outside of the United States protect CNT, and which are exclusively licensed to Medtronic in the Primary Field pursuant to the Medtronic Agreement; four issued U.S. patents and 14 issued patents in countries outside of the United States protect CNT-HF; and a further 38 patent applications were filed protecting AVIM Therapy.

In addition to customary early termination provisions, the Medtronic Agreement will terminate on the date no further revenue share payments are due under the Medtronic Agreement and Medtronic's license under the Medtronic Agreement would become fully paid up, perpetual, irrevocable and royalty-free. Revenue share payments with respect to each applicable country (or group of countries) are to be paid for a minimum period of time determined by the latest to occur of (a) the expiration of the last valid claim of certain specified patents (as well as any patents claiming priority to, from or through such patents) (the "Patent-Based Expiration") or (b) the date that is 12 years after the first commercial sale of any AVIM-enabled pacemakers in the applicable country or group of countries (the "Time-Based Revenue Share Expiration"). Accordingly, to the extent AVIM-enabled pacemakers receive regulatory approval and are sold commercially, Medtronic's obligation to make payments to us will extend to at least approximately 2041 under the Time-Based Revenue Share Expiration, regardless of the expiration of any of our patents. Further, such date may be extended up to an additional five years based on the Medtronic Agreement which provides that the Patent-Based Expiration may be extended until the expiration of patents that may be issued based on additional patent applications that we have filed prior to entering into the Medtronic Agreement, although no assurance can be given that such patents will be issued or any claims associated with newly issued patents will be valid. To the extent there are revenue share payments made under the Medtronic Agreement after the Time-Based Revenue Share Expiration and prior to the Patent-Based Expiration, those payments would likely be based on intellectual property we develop in the future, and not the current patents held by us.

AVIM Therapy and CNT-HF are also protected by trade secrets and proprietary know-how. We seek to protect its proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with its employees, consultants, scientific advisors, contractors and commercial partners.

We will continue to endeavor to obtain and maintain patent protection worldwide on select patentable aspects of AVIM Therapy and CNT-HF as well as to protect our trade secrets and proprietary know-how.

The following table lists our material patents relating to AVIM Therapy and CNT-HF as of December 31, 2025, their jurisdiction and expiration date:

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	9,008,769	8/31/2033	AVIM Therapy
United States	9,333,352	3/14/2033	AVIM Therapy
United States	9,526,900	8/31/2033	AVIM Therapy
United States	9,370,662	8/31/2033	AVIM Therapy
United States	9,656,086	3/14/2033	AVIM Therapy
United States	9,878,162	8/31/2033	AVIM Therapy
United States	9,937,351	7/4/2034	AVIM Therapy
United States	10,071,250	3/14/2033	AVIM Therapy
United States	10,252,061	8/31/2033	AVIM Therapy
United States	10,441,794	3/14/2033	AVIM Therapy
United States	10,485,658	5/16/2037	AVIM Therapy
United States	10,610,689	3/14/2033	AVIM Therapy
United States	10,967,188	7/21/2034	AVIM Therapy
United States	11,097,108	12/19/2033	AVIM Therapy
United States	11,426,589	3/17/2038	AVIM Therapy
United States	11,452,875	3/14/2033	AVIM Therapy
United States	11,712,567	8/31/2033	AVIM Therapy
United States	11,969,598	4/20/2037	AVIM Therapy
United States	11,986,661	3/14/2033	AVIM Therapy
United States	12,208,271	6/17/2034	AVIM Therapy
United States	12,246,180	6/17/2034	AVIM Therapy
United States	12,485,805	3/14/2033	AVIM Therapy
Europe	EP2934669	12/19/2033	AVIM Therapy
Great Britain	EP2934669	12/19/2033	AVIM Therapy
France	EP2934669	12/19/2033	AVIM Therapy
Germany	EP2934669	12/19/2033	AVIM Therapy
Switzerland	EP2934669	12/19/2033	AVIM Therapy
Sweden	EP2934669	12/19/2033	AVIM Therapy
Italy	EP2934669	12/19/2033	AVIM Therapy
Spain	EP2934669	12/19/2033	AVIM Therapy
Europe	EP3082949	6/17/2034	AVIM Therapy
Great Britain	EP3082949	6/17/2034	AVIM Therapy
France	EP3082949	6/17/2034	AVIM Therapy
Germany	EP3082949	6/17/2034	AVIM Therapy
Switzerland	EP3082949	6/17/2034	AVIM Therapy
Sweden	EP3082949	6/17/2034	AVIM Therapy
Europe	EP3238777	12/19/2033	AVIM Therapy
Great Britain	EP3238777	12/19/2033	AVIM Therapy
France	EP3238777	12/19/2033	AVIM Therapy
Germany	EP3238777	12/19/2033	AVIM Therapy
Switzerland	EP3238777	12/19/2033	AVIM Therapy
Sweden	EP3238777	12/19/2033	AVIM Therapy
Europe	EP3461531	6/17/2034	AVIM Therapy
Great Britain	EP3461531	6/17/2034	AVIM Therapy
France	EP3461531	6/17/2034	AVIM Therapy
Germany	EP3461531	6/17/2034	AVIM Therapy
Switzerland	EP3461531	6/17/2034	AVIM Therapy
Sweden	EP3461531	6/17/2034	AVIM Therapy
Europe	EP3639888	12/19/2033	AVIM Therapy
Great Britain	EP3639888	12/19/2033	AVIM Therapy
France	EP3639888	12/19/2033	AVIM Therapy

Jurisdiction	Patent No.	Expiration Date	Related Product
Germany	EP3639888	12/19/2033	AVIM Therapy
Switzerland	EP3639888	12/19/2033	AVIM Therapy
Sweden	EP3639888	12/19/2033	AVIM Therapy
Europe	EP3445443	4/21/2037	AVIM Therapy
Great Britain	EP3445443	4/21/2037	AVIM Therapy
France	EP3445443	4/21/2037	AVIM Therapy
Germany	EP3445443	4/21/2037	AVIM Therapy
Switzerland	EP3445443	4/21/2037	AVIM Therapy
Sweden	EP3445443	4/21/2037	AVIM Therapy
Europe	EP3954429	4/17/2041	AVIM Therapy
Great Britain	EP3954429	4/17/2041	AVIM Therapy
France	EP3954429	4/17/2041	AVIM Therapy
Germany	EP3954429	4/17/2041	AVIM Therapy
Switzerland	EP3954429	4/17/2041	AVIM Therapy
Sweden	EP3954429	4/17/2041	AVIM Therapy
China	ZL201380072479.3	12/18/2033	AVIM Therapy
China	ZL201480075987.1	6/16/2034	AVIM Therapy
China	ZL2017109301826	12/18/2033	AVIM Therapy
China	ZL2018113777986	6/16/2034	AVIM Therapy
China	ZL201780034227X	4/20/2037	AVIM Therapy
Hong Kong	HK1226016	6/16/2034	AVIM Therapy
Hong Kong	HK1243968	12/18/2033	AVIM Therapy
Australia	AU2013361318	12/19/2033	AVIM Therapy
Australia	AU2014367229	6/17/2034	AVIM Therapy
Australia	AU2018217270	12/18/2033	AVIM Therapy
Australia	AU2019204758	6/17/2034	AVIM Therapy
Australia	AU2017252310	4/21/2037	AVIM Therapy
Australia	AU2022246435	4/21/2037	AVIM Therapy
Canada	CA2893222	12/19/2033	AVIM Therapy
Canada	CA2933278	6/17/2034	AVIM Therapy
Japan	JP6457530	6/17/2034	AVIM Therapy
Japan	JP6510421	12/19/2033	AVIM Therapy
Japan	JP6381087	12/19/2033	AVIM Therapy
Japan	JP6839163	6/17/2034	AVIM Therapy
Japan	JP7050693	4/21/2037	AVIM Therapy
Japan	JP7138202	12/19/2033	AVIM Therapy
Japan	JP7222962	6/17/2034	AVIM Therapy
Japan	JP7395638	4/21/2037	AVIM Therapy
Japan	JP7672471	4/21/2037	AVIM Therapy
Japan	JP7759859	12/19/2033	AVIM Therapy
Korea	KR10-2221586	12/19/2033	AVIM Therapy
Korea	KR10-2323562	6/17/2034	AVIM Therapy
Korea	KR10-2367191	12/19/2033	AVIM Therapy
Korea	KR10-2471841	6/17/2034	AVIM Therapy
India	401318	12/19/2033	AVIM Therapy
India	409845	4/21/2037	AVIM Therapy
India	516531	4/21/2037	AVIM Therapy
India	566889	12/19/2033	AVIM Therapy
United States	7,869,874	11/7/2028	AVIM Therapy
United States	8,515,536	3/15/2028	AVIM Therapy
United States	8,340,763	3/25/2031	AVIM Therapy
United States	8,165,674	7/13/2029	AVIM Therapy
United States	8,521,280	3/1/2026	AVIM Therapy
United States	9,370,661	9/25/2030	AVIM Therapy
United States	9,427,586	11/15/2027	AVIM Therapy
United States	9,687,636	3/1/2026	AVIM Therapy
United States	9,731,136	9/8/2029	AVIM Therapy
United States	10,252,060	9/8/2029	AVIM Therapy
United States	10,369,333	9/27/2026	AVIM Therapy
United States	11,083,894	9/8/2029	AVIM Therapy
United States	11,577,059	9/27/2026	AVIM Therapy
United States	11,759,639	10/30/2029	AVIM Therapy
United States	12,239,839	9/8/2029	AVIM Therapy
United States	12,440,653	3/1/2026	AVIM Therapy
United States	8,086,315	7/3/2026	AVIM Therapy
United States	11,406,829	10/4/2026	AVIM Therapy

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	10,596,380	11/15/2027	CNT-HF
United States	11,389,658	9/8/2036	CNT-HF
United States	10,342,982	9/8/2036	CNT-HF
United States	11,529,520	11/15/2027	CNT-HF
Australia	AU2016319787	9/9/2036	CNT-HF
Japan	JP6999545	9/9/2036	CNT-HF
China	ZL2016800526048	9/9/2036	CNT-HF
Europe	EP3347090	9/9/2036	CNT-HF
Great Britain	EP3347090	9/9/2036	CNT-HF
France	EP3347090	9/9/2036	CNT-HF
Germany	EP3347090	9/9/2036	CNT-HF
Switzerland	EP3347090	9/9/2036	CNT-HF
Sweden	EP3347090	9/9/2036	CNT-HF
Italy	EP3347090	9/9/2036	CNT-HF
Spain	EP3347090	9/9/2036	CNT-HF
Korea	KR10-2630590	9/9/2036	CNT-HF
India	514118	9/9/2036	CNT-HF
Canada	CA2996312	9/9/2036	CNT-HF

Interventional Therapeutics (Virtue SAB, SirolimusEFR and Sostenocel)

We rely on intellectual property protection for Virtue SAB and its enabling technologies, including SirolimusEFR and the AngioInfusion Balloon, based on protection of proprietary particle drug encapsulation technology through trade secrets and proprietary know-how; and through issued patents and patent applications in process covering key aspects of Virtue SAB's micro-porous balloon system and integration of its drug encapsulation formulation with the device.

Virtue SAB is currently protected by 7 issued U.S. patents and 20 issued patents outside the United States with additional patent applications pending in the United States and in countries outside of the United States covering key aspects of Virtue SAB product design, clinical application and enabling technology. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2030 and 2032, without taking potential patent term extensions or adjustments into account. We will continue to selectively advance certain aspects of Virtue SAB toward submission of appropriate patent applications. A further three published patent applications were filed to protect Virtue SAB.

Our Sostenocel technology and SirolimusEFR are intentionally protected by trade secrets and proprietary know-how, as we believe the design and manufacture of this formulation would be highly difficult to develop or reverse engineer. Seeking patent protection for these processes would have required detailed publication of proprietary information without certainty of patent claim issuance or protection.

Development and production of SirolimusEFR have been refined and scaled to support the Virtue ISR-US trial and other trials we plan to conduct to support commercialization of SirolimusEFR. Production scaling and manufacturing processes are central components of the proprietary trade secret and proprietary know-how of the intellectual property protection of Virtue SAB and other future product candidates involving SirolimusEFR.

Virtue SAB is also protected by trade secrets and proprietary know-how that was intentionally not made public or published in patent applications. We believe the strategy to avoid publication of proprietary methods as long as possible has been an important part of maintaining the differentiation and advantages of Virtue SAB. Trade secrets and proprietary know-how include aspects of formulation, materials production, and manufacturing of Virtue SAB. Such trade secrets and proprietary information is used to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with its employees, consultants, scientific advisors, contractors and commercial partners.

We will continue to endeavor to obtain and maintain patent protection worldwide on select patentable aspects of Virtue SAB as well as to protect our trade secrets and proprietary know-how.

The following table lists our material patents relating to Virtue SAB as of December 31, 2025, their jurisdiction and expiration:

Jurisdiction	Patent No.	Expiration Date	Related Product
United States	8,696,644	3/9/2032	Virtue SAB
United States	8,715,230	12/30/2030	Virtue SAB
United States	9,649,478	12/30/2030	Virtue SAB
United States	9,649,479	12/30/2030	Virtue SAB
United States	10,207,084	1/6/2031	Virtue SAB
United States	10,806,909	1/6/2031	Virtue SAB
United States	12,144,945	1/6/2031	Virtue SAB
Australia	AU2010339379	12/30/2030	Virtue SAB
Australia	AU2014202452	12/30/2030	Virtue SAB
Australia	AU2016202636	12/30/2030	Virtue SAB
Australia	AU2017225072	12/30/2030	Virtue SAB
Australia	AU2019202994	12/30/2030	Virtue SAB
Australia	AU2020281081	12/30/2030	Virtue SAB
China	ZL201080064442.2	12/30/2030	Virtue SAB
Japan	JP5553908	12/30/2030	Virtue SAB
Canada	CA02786282	12/30/2030	Virtue SAB
Canada	CA3065396	12/30/2030	Virtue SAB
India	IN385350	12/30/2030	Virtue SAB
Europe	EP2603274	12/30/2030	Virtue SAB
Great Britain	EP2603274	12/30/2030	Virtue SAB
France	EP2603274	12/30/2030	Virtue SAB
Germany	EP2603274	12/30/2030	Virtue SAB
Switzerland	EP2603274	12/30/2030	Virtue SAB
Sweden	EP2603274	12/30/2030	Virtue SAB
Italy	EP2603274	12/30/2030	Virtue SAB
Spain	EP2603274	12/30/2030	Virtue SAB
Netherlands	EP2603274	12/30/2030	Virtue SAB

FreeHold Devices

Our FreeHold Devices and additional minimally invasive surgery enabling devices are protected by an intellectual property portfolio which currently includes issued U.S. patents and issued patents and pending applications in countries outside of the United States covering methods and apparatus for intracorporeal retraction and removal of organs, internal adjustment of device and retraction, as well as design for safe device removal. Specifically, this portfolio includes 10 issued U.S. patents, 12 issued patents in countries outside the United States, and one pending application. These issued patents, and any patents granted from such applications, will, or are expected to, expire between 2030 and 2037, without taking potential patent term extensions or adjustments into account. A further three published patent applications were filed to protect FreeHold devices.

Motus Devices

Our Pure-Vu® System and related highly innovative technologies rooted in systems and methods for cleaning body cavities with or without the use of an endoscope are protected by an intellectual property portfolio which includes 21 granted or allowed patents in the U.S., 20 patents in Asia (Japan, China and Hong Kong), and 13 patents in the EU, with patent protection until at least 2040. In addition, we have 6 pending patent applications in various regions of the world with a focus on the U.S., EU and Japan. We have registered trademarks for Motus GI and for the Pure-Vu® System in the U.S., EU and other international jurisdictions. We also have a pending trademark application in the U.S. to MICRO-PREP.

Government Regulation

Our AVIM Therapy and CNT-HF product candidates and our FreeHold Devices, as well as the PerQSeal and Pure-Vu products, are regulated as medical devices. Our Virtue SAB product candidate is a proprietary drug/device combination product candidate in development for the treatment of artery disease. In the United States, products composed of constituent parts that individually would be regulated under different regulatory pathways, and frequently by different centers at the FDA, are known as combination products. In the case of Virtue SAB, if marketed individually, the balloon angioplasty device would be regulated by FDA as a medical device while SirolimusEFR would be regulated by the FDA as a drug. However, under the Federal Food, Drug, and Cosmetic Act (the "FDCA"), the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The designation of a lead center generally obviates the need for separate approval of each component of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug/device combination product is attributable to the device constituent, the FDA center responsible for pre-market review of the device product would have primary jurisdiction for the combination product. A combination product with a medical-device primary mode of action generally would be reviewed and approved or cleared pursuant to the medical device approval and clearance processes set forth under the FDCA. In reviewing the marketing application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the drug component of the combination product met applicable requirements regarding safety and effectiveness. In addition, under FDA regulations, drug/device combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality Management System Regulation (the "QMSR") applicable to medical devices.

In 2019, the FDA confirmed that Virtue SAB will be regulated as a combination product candidate, with the FDA's Center for Devices and Radiological Health as the lead review center of a marketing application. We expect to seek FDA approval of each proposed indication of Virtue SAB through submission of a PMA, reviewed by the FDA's Center for Devices and Radiological Health and do not expect that the FDA will require a separate marketing authorization for each constituent component of Virtue SAB. We anticipate that our standalone SirolimusEFR product candidate for certain potential indications such as ophthalmic inflammatory conditions (uveitis) and chronic joint inflammation (osteoarthritis) will be regulated by the FDA as a drug.

Medical Device Regulation

United States

Medical devices are subject to extensive and ongoing regulation by the FDA under the FDCA and its implementing regulations, as well as other federal and state regulatory bodies in the United States and comparable authorities in other countries under other statutes and regulations. The laws and regulations govern, among other things, product design and development, preclinical and clinical testing, manufacturing, packaging, labeling, storage, recordkeeping and reporting, clearance or approval, marketing, distribution, promotion, import and export and post-marketing surveillance. Failure to comply with applicable requirements may subject a device and/or its manufacturer to a variety of administrative sanctions, such as issuance of warning letters, recalls, import detentions, suspension of manufacturing or distribution, civil monetary penalties and/or judicial sanctions, such as product seizures, injunctions and criminal prosecution.

FDA's Approval Requirements

Unless an exemption applies, each medical device commercially distributed in the United States generally requires either FDA clearance of a 510(k) pre-market notification, or approval of a PMA application. The AVIM Therapy and CNT-HF product candidates will be regulated as Class III medical devices and will require submission of a PMA supplement or a PMA. We anticipate that our Virtue SAB product candidate will be regulated as a drug/device combination product that will require submission of a PMA.

PMA Pathway

In the United States, medical devices are classified into one of three classes — Class I, Class II or Class III — depending on the degree of risk associated with each medical device and the extent of manufacturing and regulatory control needed to provide reasonable assurance of safety and effectiveness. Class I devices are deemed to be low risk and are those for which safety and effectiveness can be assured by adherence to the FDA's General Controls for medical devices, which include compliance with the applicable portions of the QMSR, facility registration and product listing, reporting of adverse medical events and truthful and non-misleading advertising and promotion. Most Class I devices are classified as exempt from pre-market notification requirements and therefore may be commercially distributed without obtaining prior authorization from the FDA. Class II devices are subject to the FDA's General Controls and special controls intended to provide reasonable assurance of safety and effectiveness of the device. Special controls can include performance standards, post-market surveillance, patient registries and guidance documents. Manufacturers of most Class II devices are required to submit to the FDA a pre-market notification under Section 510(k) of the FDCA demonstrating that the device to be marketed is as safe and effective, that is, substantially equivalent, to a legally marketed device and requesting permission to commercially distribute the device. Pursuant to the Medical Device User Fee Amendments of 2022 (MDUFA V), unless a specific exemption applies, 510(k) premarket notification submissions require payment of user fees. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, devices that utilize new technology, or devices deemed not substantially equivalent to a previously cleared 510(k) device, are placed in Class III, generally requiring approval of a PMA application.

Class III devices such as the AVIM Therapy and CNT-HF product candidates require PMA approval before they can be marketed, although some pre-amendment Class III devices for which FDA has not yet required a PMA are cleared through the 510(k) process. The PMA application process is much more demanding than the 510(k) clearance process. A PMA application must be supported by extensive data, including but not limited to technical, preclinical, clinical studies, manufacturing and labeling, to demonstrate to the FDA's satisfaction reasonable evidence of safety and effectiveness of the device. The PMA application must also contain a full description of the device and its components, a full description of the methods, facilities and controls used for manufacturing and proposed labeling. PMA applications (and supplemental PMA applications) are subject to substantially higher user fees under MDUFA V than are 510(k) premarket notifications.

After a PMA application is submitted, the FDA has 45 days to determine whether the application is sufficiently complete to permit a substantive review and thus whether the FDA will file the application for review. The FDA then has 180 days under the FDCA to review a filed PMA application, although the review of an application generally occurs over a significantly longer period of time and can take up to several years. During this review period, the FDA may request additional information or clarification of the information already provided.

Also, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. Although the FDA is not bound by the advisory panel's decision, the panel's recommendations are important to the FDA's overall decision-making process. In addition, the FDA may conduct a pre-approval inspection of the manufacturing facility to ensure compliance with the QMSR. The agency also may inspect one or more clinical sites to assure compliance with FDA's regulations.

Upon completion of the PMA review, the FDA may: (i) approve the PMA which authorizes commercial marketing with specific prescribing information for one or more indications, which can be more limited than those originally sought; (ii) issue an approvable letter which indicates the FDA's belief that the PMA is approvable and states what additional information the FDA requires, or the post-approval commitments that must be agreed to prior to approval; (iii) issue a "not approvable" letter which outlines steps required for approval, but which are typically more onerous than those in an approvable letter, and may require additional clinical studies that are often expensive and time consuming and can delay approval for months or even years; or (iv) deny the application. If the FDA issues an approvable or not approvable letter, the applicant has 180 days to respond, after which the FDA's review clock is reset.

The FDA will generally approve the new device for commercial distribution if it determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for the use(s) indicated in the proposed labeling. The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and collection of long-term follow-up data from patients in the clinical study that supported PMA approval or requirements to conduct additional clinical studies post-approval. The FDA may condition PMA approval on some form of post-market surveillance when deemed necessary to protect the public's health or to provide additional safety and efficacy data for the device in a larger population or for a longer period of use. In such cases, the manufacturer might be required to follow certain patient groups for a number of years and to make periodic reports to the FDA on the clinical status of those patients. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval.

Certain changes to an approved device, such as changes in manufacturing facilities, methods, or quality control procedures, or changes in the design performance specifications, which affect the safety or effectiveness of the device, require submission of a PMA supplement. PMA supplements often require submission of the same type of information as a PMA, except that the supplement is limited to information needed to support any changes from the device covered by the original PMA and may not require as extensive clinical data or the convening of an advisory panel. Certain other changes to an approved device require the submission of a new PMA, such as when the design change causes a different intended use, mode of operation, and technical basis of operation, or when the design change is so significant that a new generation of the device will be developed, and the data that were submitted with the original PMA are not applicable for the change in demonstrating a reasonable assurance of safety and effectiveness.

Clinical Studies

Clinical studies are almost always required to support pre-market approval and are sometimes required for 510(k) clearance. All clinical investigations of investigational devices designed to determine safety and effectiveness must be conducted in accordance with the FDA's IDE regulations, which govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk" to human health, as defined by the FDA, the FDA requires the device sponsor to submit an IDE application to the FDA, which must become effective prior to commencing human clinical studies. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE will automatically become effective 30 days after receipt by the FDA unless the FDA notifies the company that the investigation may not begin. If the FDA determines that there are deficiencies or other concerns with an IDE for which it requires modification, the FDA may permit a clinical study to still proceed under a conditional approval. Acceptance of an IDE for review does not guarantee that the FDA will allow the IDE to become effective and, if it does become effective, the FDA may or may not determine that the data derived from the trials support the safety and effectiveness of the device or warrant the continuation of clinical studies.

Regardless of the degree of risk presented by the medical device, clinical studies must be approved by, and conducted under the oversight of, an Institutional Review Board (IRB), for each clinical study site. An IRB is an appropriately constituted group that has been formally designated to review and monitor medical research involving subjects and which has the authority to approve, require modifications in, or disapprove research to protect the rights, safety and welfare of human research subjects. If an IDE application is approved by the FDA and one or more IRBs, human clinical studies may begin at a specific number of investigational sites with a specific number of patients, as approved by the FDA. If the evaluation of the device presents a non-significant risk to the patient, a sponsor may begin the clinical study after obtaining approval for the study by one or more IRBs without separate approval from the FDA. However, the clinical study must still be conducted in compliance with abbreviated IDE and human subject protection requirements, such as monitoring the investigation, ensuring that the investigators obtain informed consent, and labeling and recordkeeping requirements. During a study, the sponsor is required to comply with the applicable FDA requirements, including, for example, trial monitoring, selecting clinical investigators and providing them with the investigational plan, ensuring IRB review, adverse event reporting, recordkeeping, and prohibitions on the promotion of investigational devices or on making safety or effectiveness claims for them. The clinical investigators in the clinical study are also subject to FDA regulations and must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and recordkeeping requirements. Additionally, after a trial begins, the sponsor, the FDA or the IRB could suspend or terminate a clinical study at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits, or failures to follow applicable regulations.

Sponsors of certain clinical studies of medical devices are required to register their studies with clinicaltrials.gov, a public database of clinical study information. Information related to the device, patient population, phase of investigation, study sites and investigators and other aspects of the clinical study is made public as part of the registration.

Breakthrough Devices Program

Following passage of the 21st Century Cures Act, the FDA implemented the Breakthrough Devices Program, which is a voluntary program offered to manufacturers of certain medical devices and device-led combination products that may provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The goal of the program is to provide patients and healthcare providers with more timely access to qualifying devices by expediting their development, assessment and review, while preserving the statutory standards for PMA approval, 510(k) clearance and de novo classification. The program is available to medical devices that meet certain eligibility criteria, including that the device provides more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, and that the device meets one of the following criteria: (i) the device represents a breakthrough technology, (ii) no approved or cleared alternatives exist, (iii) the device offers significant advantages over existing approved or cleared alternatives, or (iv) the availability of the device is in the best interest of patients. Breakthrough Device designation provides certain benefits to device developers, including more interactive and timely communications with FDA staff, use of post-market data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device, opportunities for efficient and flexible clinical study design, and prioritized review of premarket submissions.

Ongoing Regulation by the FDA

Even after a device receives clearance or approval and is placed on the market, numerous regulatory requirements apply. These include:

- establishment registration and device listing;
- labeling regulations, which require that promotion is truthful, not misleading, fairly balanced, provides adequate directions for use, and that all claims are substantiated, and the FDA prohibitions against the promotion of products for uncleared, unapproved or "off-label" uses and other requirements related to promotional activities;
- medical device reporting regulations, which require that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury, or if their device malfunctioned and the device or a similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur;

- corrections and removal reporting regulations, which require that manufacturers report to the FDA field corrections or removals if undertaken to reduce a risk to health posed by a device or to remedy a violation of the FDCA that may present a risk to health;
- requirements for Unique Device Identifiers on devices and the submission of certain information about each device to the FDA's Global Unique Device Identification Database;
- the FDA's recall authority, whereby the FDA can order device manufacturers to recall a medical device from the market if the FDA finds that there is a reasonable probability that the device would cause serious, adverse health consequences or death; and
- post-market surveillance regulations, which apply to certain Class II or Class III devices when necessary to protect the public's health or to provide additional safety and effectiveness data for the device.

Manufacturing of medical devices is required to comply with the applicable portions of the QMSR, which cover the methods and the facilities, controls for the design, manufacture, testing, production, processes, controls, quality assurance, labeling, packaging, distribution, installation, and servicing of finished devices intended for human use. The QMSR also requires, among other things, maintenance of a device master file, device history file, and complaint files. The QMSR incorporates by reference requirements of the international standard specific for medical device quality management systems set by the International Organization for Standardization (ISO), ISO 13485:2016. Our facilities, records, and manufacturing processes, as well as those of our contract manufacturers, are subject to periodic scheduled or unscheduled inspections by the FDA. Our or our contract manufacturers' failure to maintain compliance with the QMSR or other applicable regulatory requirements could result in the shut-down of, or restrictions on, its manufacturing operations and the recall or seizure of its products. The discovery of previously unknown problems with any marketed products, including unanticipated adverse events or adverse events of increasing severity or frequency, whether resulting from the use of the device within the scope of its clearance or off-label by a physician in the practice of medicine, could result in restrictions on the device, including the removal of the product from the market or voluntary or mandatory device recalls.

The FDA has broad regulatory compliance and enforcement powers. If the FDA determines that a manufacturer has failed to comply with applicable regulatory requirements, it can take a variety of compliance or enforcement actions, which may result in any of the following sanctions:

- warning or untitled letters, fines, injunctions, consent decrees and civil penalties;
- customer notifications, voluntary or mandatory recall or seizure of products;
- operating restrictions, partial suspension or total shutdown of production;
- refusals or delays in processing submissions or applications for new products or modifications to existing products;
- refusal to grant export or import approvals for products;
- withdrawing approvals that have already been granted; and
- criminal prosecution.

European Union

We believe our Virtue SAB, AVIM Therapy and CNT-HF product candidates as well as our FreeHold Devices would be regulated in the EU as medical devices.

The EU has adopted specific directives and regulations regulating the design, manufacture, clinical investigation, conformity assessment, labeling and adverse event reporting for medical devices (including active implantable medical devices).

Until May 25, 2021, medical devices (including active implantable medical devices) were regulated by Council Directive 93/42/EEC and Council Directive 90/385/EEC (the "EU Medical Devices Directives"), which have been repealed and replaced by Medical Devices Regulation (EU) No 2017/745 (the "EU Medical Devices Regulation"). Our current certificates have been granted under the EU Medical Devices Directives whose regimes are described below. However, as of May 26, 2021, some of the EU Medical Devices Regulation requirements apply in place of the corresponding requirements of the EU Medical Devices Directives with regard to registration of economic operators and of devices, post-market surveillance and vigilance requirements. If we want to market our medical devices in the EU, it will notably require that our devices be certified under the new regime set forth in the EU Medical Devices Regulation.

Medical Devices Directives

Under the EU Medical Devices Directives, all medical devices (including active implantable medical devices) placed on the market in the EU must meet the relevant essential requirements laid down in Annex I to the EU Medical Devices Directives, including the requirement that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performance intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. The European Commission has adopted various standards applicable to medical devices. These include standards governing common requirements, such as sterilization and safety of medical electrical equipment and product standards for certain types of medical devices. There are also harmonized standards relating to design and manufacture. While not mandatory, compliance with these standards is viewed as the easiest way to satisfy the essential requirements as a practical matter as it creates a rebuttable presumption that the device satisfies that essential requirement.

To demonstrate compliance with the essential requirements laid down in Annex I to the EU Medical Devices Directives, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. As a general rule, demonstration of conformity of medical devices and their manufacturers with the essential requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-assess the conformity of its products with the essential requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a notified body. Notified bodies are independent organizations designated by EU member states to assess the conformity of devices before being placed on the market. A notified body would typically audit and examine a product's technical dossiers and the manufacturers' quality system (the notified body must presume that quality systems which implement the relevant harmonized standards — which is ISO 13485:2016 for Medical Devices Quality Management Systems — conform to these requirements). If satisfied that the relevant product conforms to the relevant essential requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EU.

Throughout the term of the certificate of conformity, the manufacturer will be subject to periodic surveillance audits to verify continued compliance with the applicable requirements. In particular, there will be a new audit by the notified body before it will renew the relevant certificate(s).

Medical Devices Regulation

The regulatory landscape related to medical devices in the EU recently evolved. On April 5, 2017, the EU Medical Devices Regulation was adopted with the aim of ensuring better protection of public health and patient safety. The EU Medical Devices Regulation establishes a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. Unlike the EU Medical Devices Directives, the EU Medical Devices Regulation is directly applicable in EU member states without the need for member states to implement into national law. This aims at increasing harmonization across the EU.

The EU Medical Devices Regulation became effective on May 26, 2021. The new regulation, among other things:

- strengthens the rules on placing devices on the market (e.g., reclassification of certain devices and wider scope than the EU Medical Devices Directives) and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- establishes explicit provisions on importers' and distributors' obligations and responsibilities;
- imposes an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;
- sets up a central database (Eudamed) to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo a clinical evaluation consultation procedure by experts before they are placed on the market.

Devices lawfully placed on the market pursuant to the EU Medical Devices Directives prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025, provided that the requirements of the transitional provisions are fulfilled. In particular, the certificate in question must still be valid. However, even in this case, manufacturers must comply with a number of new or reinforced requirements set forth in the EU Medical Devices Regulation, in particular the obligations described below. The EU Medical Devices Regulation requires that before placing a device, other than a custom-made device, on the market, manufacturers (as well as other economic operators such as authorized representatives and importers) must register by submitting identification information to the electronic system (Eudamed), unless they have already registered. The information to be submitted by manufacturers (and authorized representatives) also includes the name, address and contact details of the person or persons responsible for regulatory compliance. The new regulation also requires that before placing a device, other than a custom-made device, on the market, manufacturers must assign a unique identifier to the device and provide it along with other core data to the unique device identifier ("UDI") database. These new requirements aim at ensuring better identification and traceability of the devices. Each device — and as applicable, each package — will have a UDI composed of two parts: a device identifier specific to a device, and a production identifier to identify the unit producing the device. Manufacturers are also notably responsible for entering the necessary data on Eudamed, which includes the UDI database, and for keeping it up to date. The obligations for registration in Eudamed will become applicable at a later date (as Eudamed is not yet fully functional). Until Eudamed is fully functional, the corresponding provisions of the EU Medical Devices Directive continue to apply for the purpose of meeting the obligations laid down in the provisions regarding exchange of information, including, and in particular, information regarding registration of devices and economic operators.

All manufacturers placing medical devices on the market in the EU must comply with the EU medical device vigilance system which has been reinforced by the EU Medical Devices Regulation. Under this system, serious incidents and Field Safety Corrective Actions ("FSCAs") must be reported to the relevant authorities of the EU member states. These reports will have to be submitted through Eudamed — once functional — and aim to ensure that, in addition to reporting to the relevant authorities of the EU member states, other actors such as the economic operators in the supply chain will also be informed. Until Eudamed is fully functional, the corresponding provisions of the EU Medical Devices Directives continue to apply. A serious incident is defined as any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect, which, directly or indirectly, might have led or might lead to the death of a patient or user or of other persons or to a temporary or permanent serious deterioration of a patient's, user's or other person's state of health or a serious public health threat. Manufacturers are required to take FSCAs defined as any corrective action for technical or medical reasons to prevent or reduce risk of a serious incident associated with the use of a medical device that is made available on the market. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its legal representative to its customers and/or to the end users of the device through Field Safety Notices. For similar serious incidents that occur with the same device or device type and for which the root cause has been identified or a FSCA implemented or where the incidents are common and well documented, manufacturers may provide periodic summary reports instead of individual serious incident reports.

The advertising and promotion of medical devices is subject to some general principles set forth in EU legislation. According to the EU Medical Devices Regulation, only devices that are CE-marked may be marketed and advertised in the EU in accordance with their intended purpose. Directive 2006/114/EC concerning misleading and comparative advertising and Directive 2005/29/EC on unfair commercial practices, while not specific to the advertising of medical devices, also apply to the advertising thereof and contain general rules, for example, requiring that advertisements are evidenced, balanced and not misleading. Specific requirements are defined at a national level. EU member states' laws related to the advertising and promotion of medical devices, which vary between jurisdictions, may limit or restrict the advertising and promotion of products to the general public and may impose limitations on promotional activities with healthcare professionals.

Many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medical devices, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on medical device manufacturers. Certain countries also mandate implementation of commercial compliance programs.

The aforementioned EU rules are generally applicable in the European Economic Area (the "EEA"), which consists of the 27 EU Member States plus Norway, Liechtenstein and Iceland.

United Kingdom

In the United Kingdom ("UK"), the medical devices market is regulated by the Medicines and Healthcare products Regulatory Agency, which performs market surveillance of medical devices on the UK market. Devices are regulated under the Medical Devices Regulations 2002, which gave effect in UK law to the following EU directives: Directive 90/385/EEC on active implantable medical device; Directive 93/42/EEC on medical devices; and Directive 98/79/EC on in vitro diagnostic medical devices. The UK Conformity Assessed ("UKCA") marking is a UK product marking used for medical devices being placed on the Great Britain market. It is not recognized in the EU, so these products require a CE marking as well. CE marketed devices will be accepted on the Great Britain market until June 30, 2023. From July 1, 2023, devices placed on the Great Britain market will need to conform to UKCA marketing requirements.

We may need to support clinical and/or regulatory requirements in the UK for its AVIM Therapy product candidate, and potentially others.

Other Regions

Most major markets have different levels of regulatory requirements for medical devices. Modifications to the approved or certified products may require a new regulatory submission in all major markets. The regulatory requirements, and the review time, vary significantly from country to country. Products can also be marketed in other countries that have minimal requirements for medical devices.

Drug Regulation

United States

In the United States, our SirolimusEFR product candidate is subject to extensive regulation by the FDA, which regulates drugs under the FDCA and its implementing regulations, and other federal, state, and local regulatory authorities. The process of obtaining regulatory approvals and certifications and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;
- submission to the FDA of an investigational new drug ("IND") application, which must become effective before human clinical studies may begin;
- approval by an independent IRB or ethics committee at each clinical site before each trial may be initiated;
- generation of data from adequate and well-controlled human clinical studies in accordance with Good Clinical Practice ("GCP") requirements to establish the safety and efficacy of the proposed drug product for its intended use;
- submission to the FDA of a new drug application (an "NDA") after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data, if applicable;
- payment of user fees; and
- FDA review and approval of the NDA.

We have performed CMC testing in support of our IDE approval for the combination product Virtue SAB that includes populating a DMF. We intend to follow up post-IDE approval for the Virtue SAB with exploring additional pre-clinical work to support additional indications. Depending on the indication, we may be able to leverage some of the biocompatibility and CMC data in the DMF, while providing additional data depending on the indication selected.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective and a clinical study proposed in the IND may begin 30 days after the FDA receives the IND, unless before that time the FDA raises concerns or questions related to one or more proposed clinical studies and places the clinical study on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. As a result, submission of an IND may not result in the FDA allowing clinical studies to commence.

We believe that additional preclinical studies will be necessary for evaluating SirolimusEFR in new indications.

Clinical Studies

Clinical studies involve the administration of the new investigational drug to human subjects under the supervision of qualified investigators in accordance with GCP and human subject protection requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IRB at each institution participating in the clinical study must review and approve the plan for any clinical study before it commences at that institution, and the IRB must continue to oversee the clinical study while it is being conducted. Some trials also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a Data Safety Monitoring Board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical study based on prespecified criteria, for example, if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Information about certain clinical studies must be submitted within specific timeframes for public dissemination on the *www.clinicaltrials.gov* website.

Human clinical studies are typically conducted in three or four sequential phases, which may overlap or be combined:

- *Phase 1:* The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- *Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* The drug is administered to an expanded patient population, generally at geographically dispersed clinical study sites, in well-controlled clinical studies to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- *Phase 4:* In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical studies after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical studies post-approval to gain more information about the drug. Certain post-approval trials may be typically referred to as Phase 4 clinical studies.

Progress reports detailing the results of the clinical studies, among other information, must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Furthermore, the FDA or the sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk or the failure to meet the trial's objectives. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

We believe that additional clinical studies will be necessary for evaluating SirolimusEFR in new indications.

Marketing Approval

Assuming successful completion of the required clinical testing in accordance with all applicable regulatory requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act guidelines that are currently in effect, the FDA has a goal of 10 months to review and act on an NDA designed for standard review and six months to review and act on an NDA designed for priority review, measured from the "filing" date for an NDA for a new molecular entity ("NME") or from the receipt date for an NDA for a non-NME product. Measuring from the "filing" date typically adds approximately two months to the timeline for review and decision, because the FDA has sixty days from receipt to make a "filing" decision, as described below.

In addition, under the Pediatric Research Equity Act of 2003 as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements as relevant.

Under certain circumstances, the FDA also may require submission of a risk evaluation and mitigation strategy ("REMS") plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical study sites to assure compliance with GCP requirements.

The FDA generally accepts data from foreign clinical studies in support of an NDA if the trials were conducted under an IND. If a foreign clinical study is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an on-site inspection, if deemed necessary. The FDA may accept foreign clinical data as the sole clinical basis for marketing approval if (1) the foreign data are demonstrated to be applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical study sites, if any, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter contains a statement of all deficiencies identified in the NDA and the specific conditions that must be met to secure final approval of the NDA and may require additional clinical testing, preclinical testing, manufacturing or formulation modifications or other changes in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that a resubmitted application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications or other conditions of use for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical studies, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may take steps to prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, may be subject to further testing requirements and FDA review and approval.

SirolimusEFR is the drug product component of our combination product Virtue SAB. On April 29, 2025, we announced that we had received FDA approval for an IDE amendment to initiate an updated design of our planned Virtue Trial for our Virtue SAB product candidate for the treatment of Coronary ISR.

The Hatch-Waxman Amendments

Our current regulatory strategy is to pursue development of a standalone SirolimusEFR product candidate for potential indications such as ophthalmic inflammatory conditions (uveitis) and chronic joint inflammation (osteoarthritis) as a Section 505(b)(2) NDA. As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on the FDA's previous findings of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by or for the applicant and for which the applicant does not contain a right of reference. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the product candidate. The FDA may also require companies to perform additional bridging studies or measurements, including clinical studies, to support the change from the approved listed drug. The FDA may then approve the new product candidate for all, or some, of the labeled indications and conditions of use for which the listed drug has been approved, as well as for any new indications and conditions of use sought by the 505(b)(2) applicant.

Orange Book Listing

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, known as the Orange Book. Any applicant who files an Abbreviated New Drug Application ("ANDA") seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify, for each patent listed in the Orange Book for the referenced drug, to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) the date on which such patent expires or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. The fourth certification described above is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. This section viii statement does not require notice to the patent holder or NDA owner. There might also be no relevant patent certification.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the applicant. Even if the 45 days expire, a patent infringement lawsuit can be brought and could delay market entry, but it would not extend the FDA-related 30-month stay of approval.

The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired. Specifically, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. During the five-year NCE exclusivity period, the FDA cannot accept for filing and cannot approve any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that the FDA may accept an application for filing after four years (and may initiate a review of the application, but still may not approve it for five years) if the follow-on applicant makes a paragraph IV certification. This exclusivity period may be extended by an additional six months if certain requirements are met to qualify the product for pediatric exclusivity, including the receipt of a written request from the FDA that the NDA holder conduct certain pediatric studies, the submission of study reports from such studies to the FDA after receipt of the written request and satisfaction of the conditions specified in the written request.

In addition, a drug, including one approved under Section 505(b)(2), may also obtain a three-year period of market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/ sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application that relies on the information supporting the approval of the drug, or the change to the drug for which the information was submitted and the exclusivity granted, until after that three-year exclusivity period has run. However, unlike for NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA and other government authorities, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, product tracking and tracing, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to prior FDA review and approval. There also are continuing annual program fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical studies, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state authorities and are subject to periodic unannounced inspections by the FDA and these state authorities for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if certain conditions are met, for example, if clinical or other experience, tests, or other scientific data show that such drug is unsafe for use. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution or other restrictions under a REMS program.

Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product or complete withdrawal of the product from the market;
- fines, warning letters or holds on ongoing or proposed clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. A company generally can make only claims with respect to FDA-approved uses of a drug and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (the "PDMA"), which regulates the distribution of drug samples at the federal level. Title II of the Federal Drug Quality and Security Act of 2013, known as the Drug Supply Chain Security Act (DSCSA), has also imposed "track and trace" requirements on the distribution of prescription drug products by manufacturers, distributors, and other entities in the drug supply chain. The DSCSA requires product identifiers (*i.e.*, serialization) on prescription drug products in order to establish an electronic interoperable system to identify and trace certain prescription drugs distributed in the United States and preempts existing state drug pedigree laws and regulations on this topic.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical studies and commercial sales and distribution of its products. Whether or not we obtain FDA approval for a product, it must obtain approval or certification by the comparable regulatory authorities of foreign countries before it can commence clinical studies, and approval or certification from regulatory authorities in foreign countries, such as the EU, before it may market products in those countries. The requirements and process governing the conduct of clinical studies, approval process, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical studies

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical studies of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization's GCPs, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical study is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical study insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical study.

The regulatory landscape related to clinical study in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR"), which was adopted in April 2014 and repeals the EU Clinical Trials Directive (the "Clinical Trials Directive"), became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical studies throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical studies will be governed by the CTR varies. For clinical studies whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical studies must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MA" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Product for Human Use ("CHMP") of the European Medicines Agency ("EMA") and are valid throughout the EU. The centralized procedure is mandatory for certain types of product candidates, such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicines, (iii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases and (iv) advanced therapy medicinal products such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days.

In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical study designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Data and marketing exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical study data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAAs must include a risk management plan describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical studies or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

Failure to comply with EU and member state laws that apply to the conduct of clinical studies, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical studies, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical studies, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Regulation of Combination Products in the EU

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework.

Drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. The EMA is responsible for evaluating the quality, safety and efficacy of MAAs submitted through the centralized procedure, including the safety and performance of the medical device in relation to its use with the medicinal product. The EMA or the EU member state national competent authority will assess the product in accordance with the rules for medicinal products described above but the device part must comply with the EU Medical Devices Regulation (including the general safety and performance requirements provided in Annex I). The MAA must include — where available — the results of the assessment of the conformity of the device part with the Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the competent authority must require the applicant to provide a notified body opinion on the conformity of the device.

By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the EU Medical Devices Regulation.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product.

The requirements regarding quality documentation for medicinal products when used with a medical device, including single integral products, co-packaged and referenced products, are outlined in the EMA guideline of July 22, 2021, which became applicable as of January 1, 2022.

The aforementioned EU rules are generally applicable in the EEA.

Coverage and Reimbursement

Sales of any pharmaceutical and medical device product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for medical devices, pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical devices and pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Fraud and Abuse and Other Healthcare Regulations

Federal and state governmental agencies and equivalent foreign authorities subject the healthcare industry to intense regulatory scrutiny, including heightened civil and criminal enforcement efforts. These laws constrain the sales, marketing and other promotional activities of medical device manufacturers by limiting the kinds of financial arrangements we may have with hospitals, physicians and other potential purchasers of its products. Federal healthcare fraud and abuse laws apply to our business when a customer submits a claim for an item or service that is reimbursed under Medicare, Medicaid or other federally funded healthcare programs. Patient privacy statutes and regulations by foreign, federal and state governments may also apply in the locations in which we do business. Descriptions of some of the U.S. laws and regulations that may affect our ability to operate follow.

Federal Healthcare Anti-Kickback Statute

The federal Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value, and the government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the law or a specific intent to violate it. In addition, the government may assert that a claim, including items or services resulting from a violation of the Anti-Kickback Statute, constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The Anti-Kickback Statute is subject to evolving interpretations and has been applied by government enforcement officials to a number of common business arrangements in the medical device industry. There are a number of statutory exceptions and regulatory safe harbors protecting certain business arrangements from prosecution under the Anti-Kickback Statute; however, those exceptions and safe harbors are drawn narrowly and there is no exception or safe harbor for many common business activities, such as reimbursement support programs, educational and research grants or charitable donations. The failure of a transaction or arrangement to fit precisely within one or more applicable statutory exceptions or regulatory safe harbors does not necessarily mean that it is illegal or that prosecution will be pursued. However, conduct and business arrangements that do not fully satisfy all requirements of an applicable safe harbor may result in increased scrutiny by government enforcement authorities and will be evaluated on a case-by-case basis based on a cumulative review of all facts and circumstances.

Federal Civil False Claims Act

The federal civil False Claims Act prohibits, among other things, persons or entities from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government. A claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Actions under the federal civil False Claims Act may be brought by the government or as a qui tam action by a private individual in the name of the government. These individuals, sometimes known as "relators" or, more commonly, as "whistleblowers," may share in any amounts paid by the entity to the government in fines or settlement. The number of filings of qui tam actions has increased significantly in recent years. Qui tam actions are filed under seal and impose a mandatory duty on the U.S. Department of Justice to investigate such allegations. Most private citizen actions are declined by the Department of Justice or dismissed by federal courts. However, the investigation costs for a company can be significant and material even if the allegations are without merit. Various states have adopted laws similar to the federal civil False Claims Act, and many of these state laws are broader in scope and apply to all payors, and therefore, are not limited to only those claims submitted to the federal government. Medical device manufacturers and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

Healthcare Fraud Statute

The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 1996 ("HIPAA") and its implementing regulations created federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Sunshine Act

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually with certain exceptions to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (as defined by statute), certain non-physician practitioners, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives, and teaching hospitals, either directly or indirectly through a third party at the request of such physician, non-physician practitioner or teaching hospital, as well as ownership and investment interests held by physicians and their immediate family members.

Other State Laws

Certain states also mandate implementation of commercial compliance programs, impose restrictions on device manufacturer marketing practices and/or require tracking and reporting of gifts, compensation and other remuneration to healthcare professionals and entities.

State and federal regulatory and enforcement agencies continue to actively investigate violations of healthcare laws and regulations, and the U.S. Congress continues to strengthen the arsenal of enforcement tools. The Bipartisan Budget Act of 2018 (the "BBA") increased the criminal and civil penalties that can be imposed for violating certain federal healthcare laws, including the Anti-Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular, government agencies recently have increased regulatory scrutiny and enforcement activity with respect to manufacturer reimbursement support activities and other patient support programs, including bringing criminal charges or civil enforcement actions under the Anti-Kickback Statute, federal civil False Claims Act and violations of healthcare fraud and HIPAA privacy provisions.

Enforcement and Penalties for Noncompliance with Fraud and Abuse Laws and Regulations

Compliance with these federal and state laws and regulations requires substantial resources. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to it, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from participation in government healthcare programs such as the Medicare and Medicaid programs, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of its operations. Companies settling federal civil False Claims Act, Anti-Kickback Statute and other fraud and abuse cases also may be required to enter into a Corporate Integrity Agreement with the U.S. Department of Health and Human Services Office of Inspector General in order to avoid exclusion from participation *(i.e.*, loss of coverage for their products) in federal healthcare programs such as Medicare and Medicaid. Corporate Integrity Agreements typically impose substantial costs on companies to ensure compliance.

For additional information regarding obligations under federal healthcare statues and regulations, please see the section titled *"Risk Factors — Risks Related to Government Regulation and Our Industry — Our relationships with physicians, patients and payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, and other healthcare laws and regulations."*

United States Healthcare Reform

There have been and continue to be proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of healthcare and, more generally, to reform the U.S. healthcare system.

For example, in the United States, in March 2010, the Patient Protection and the Affordable Care Act, as amended by the Health Care and Education and Reconciliation Act (collectively, the "ACA"), was enacted. The ACA contained a number of significant provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which impacted existing government healthcare programs and resulted in the development of new programs. The ACA also imposed an excise tax of 2.3% on the sale of most medical devices, which was suspended, effective January 1, 2016, and subsequently repealed, effective January 1, 2020.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, includes reductions to Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2032, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Inflation Reduction Act of 2022 included, among other things, provisions that impose new manufacturer financial liability on certain drugs under Medicare Part D, allowing the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition. Similarly, the One Big Beautiful Bill Act of 2025 will reduce Medicaid funding significantly.

Further, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to bring transparency to product pricing and reduce the cost of products and services under government healthcare programs. Additionally, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what products to purchase and which suppliers will be included in their healthcare programs.

We expect additional state, federal and foreign healthcare reform measures to be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure.

For instance, in December 2021, the EU Regulation No 2021/2282 on Health Technology Assessment (the "HTA"), amending Directive 2011/24/EU, was adopted. This regulation which entered into force in January 2022 intends to boost cooperation among EU member states in assessing health technologies, including some medical devices, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Our Employees

As of December 31, 2025, we had 86 employees engaged in finance, clinical, research and development, engineering, regulatory and administration functions. We anticipate that the number of employees will grow as we scale our research and development and clinical organizational capabilities. In addition, we utilize and will continue to utilize consultants, clinical research organizations and third parties to perform our analytical and test method development, component and sub-assembly design and manufacturing, as well as preclinical studies, clinical studies, manufacturing and regulatory functions. We will use consultants and third-party analytical and design houses to complement internal capabilities and will utilize external manufacturing partners that have extensive experience in medical devices and dealing with regulatory bodies to provide components, assemblies and final product. Our suppliers will have ISO 13485 approved quality systems (or have been approved for GMP manufacturing of pharmaceutical products).

None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our employee relations to be good.

Available Information

We maintain a website at www.orchestrabiomed.com. We are providing the address to our website solely for the information of investors. The information contained on, or accessible through, our website is not a part of, nor is it incorporated by reference into this Form 10-K. Through our website, we make available, free of charge, our annual proxy statement, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act of 1934, as amended (the "Exchange Act"), as soon as reasonably practicable after we electronically file such material with, or furnish it to the SEC. The SEC maintains a website that contains these reports at www.sec.gov.

Item 1A. Risk Factors

Our business involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as other information included in this Annual Report on Form 10-K, including our audited consolidated financial statements and related notes appearing in Item 8 of this Annual Report on Form 10-K. The risks described below are not the only ones facing us. The occurrence of any of the following risks or additional risks and uncertainties not presently known to us or that we currently believe to be immaterial could materially and adversely affect our business, financial condition or results of operations. In such case, the trading price of our common stock could decline, and you may lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements and estimates that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of specific factors, including the risks and uncertainties described below.

Risks Related to Our Business and Products

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

We have incurred losses since our inception and expect to continue to incur losses for the foreseeable future. We have reported a net loss of $52.7 million for the year ended December 31, 2025 and a net loss of $61.0 million for the year ended December 31, 2024. As a result of these losses, as of December 31, 2025, we had an accumulated deficit of approximately $362.6 million. We expect to continue to incur net losses for the foreseeable future.

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

We may need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses may increase substantially in connection with our ongoing and planned activities, particularly as we conduct our ongoing BACKBEAT study and Virtue Trial. Furthermore, we have incurred and will continue to incur additional costs associated with operating as a public company. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our research and development efforts.

The amount and timing of our future funding requirements are dependent on many factors, including the cost and pace of execution of clinical studies and research and development activities, the strength of results from clinical studies and other research, development and manufacturing efforts, as well as the potential receipt of revenues or other payments or investments under the Medtronic Agreement and/or future collaborations, and the realization of cash from the acquisition of Vivasure by Haemonetics.

We had $34.7 million in cash and cash equivalents at December 31, 2025, which consisted primarily of bank deposits and money market funds. We also had $71.8 million of short-term marketable securities at December 31, 2025, which consisted primarily of our investments in corporate debt securities.

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

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

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

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

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

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development and commercialization goals, which we sometimes refer to as milestones. These milestones include the commencement or completion of scientific studies and clinical studies and the submission of regulatory applications. We base these milestones on a variety of assumptions, which are subject to numerous risks and uncertainties. Our future collaboration agreements may have similar provisions. There is a risk we will not achieve these milestones on a timely basis or at all. Even if we achieve these milestones, the actual timing of the achievement of these milestones can vary dramatically compared to our estimates, often for reasons beyond our control, depending on numerous factors, including:

- our ability and/or the ability of third-party vendors and partners to manufacture our product candidates;
- our ability to source critical components or materials for the manufacture of our product candidates;
- the rate of progress, costs and results of our clinical studies and research and development activities;
- our ability to identify and enroll patients who meet clinical study eligibility criteria;
- the extent of scheduling conflicts with participating physicians and clinical institutions;
- adverse reactions reported during clinical studies or commercialization;
- the ability of our product candidates to meet the standards for regulatory approval or certification;
- the receipt of marketing approvals, clearances or certifications by our competitors and by us from the FDA and other regulatory agencies or notified bodies; and
- other actions by regulators, including actions related to a class of products.

If we do not meet these milestones for our products or if we are delayed in achieving these milestones, the development and commercialization of new product candidates, modifications of existing products or sales of existing products for new indications may be prevented or delayed, which could damage our reputation or materially adversely affect our business. Further, we may not receive milestone-based payments from partners on a timely basis or at all, which may have an adverse impact on our anticipated financial resources.

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

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

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

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

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

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

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

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

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

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

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

The FDA and comparable foreign regulatory authorities may not accept data from any preclinical or clinical trials we may conduct in foreign countries.

Up to 50% of our BACKBEAT study data is expected to come from sites or patients outside of the United States. While we remain in compliance with the parameters the FDA has set for us regarding clinical data received from abroad in the BACKBEAT study, the FDA's acceptance of data generated for patients recruited outside the United States from clinical trials conducted in whole or in part outside the United States may be subject to certain conditions.

Although the FDA has the authority to accept foreign data as part or even the sole basis for marketing approval, the FDA generally does not approve an application on the basis of foreign data alone unless (i) the data is applicable to the U.S. population and U.S. medical practice, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations, and (iii) the FDA's clinical trial requirements were met. Many foreign regulatory authorities have similar approval requirements. In addition, any clinical study conducted in whole or in part outside of the United States would be subject to the applicable local laws of the jurisdiction where the trial was conducted. We cannot guarantee that the FDA or comparable foreign regulatory authority will accept data from trials conducted in whole or in part outside of the United States, which may result in the need for additional trials conducted in the United States.

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

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

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

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

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

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

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

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

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

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

- the level of demand for our products and any approved or certified products, which may vary significantly;
- expenditures that we may incur to acquire, develop or commercialize additional products and technologies;
- the ability to obtain, and timing and cost of obtaining regulatory approvals or certifications for planned or future products or indications;
- the degree of competition in our industry and any change in the competitive landscape of our industry, including consolidation among our competitors or future partners;

- coverage and reimbursement policies with respect to our products, if approved or certified, and potential future products that compete with our products;
- the timing and success or failure of preclinical studies or clinical studies for our products or any future products we develop or competing products;
- the timing of customer orders or medical procedures using our products and the number of available selling days in any quarterly period, which can be impacted by holidays, the mix of products sold and the geographic mix of where products are sold;
- the timing and cost of, and level of investment in, research, development, regulatory approval or certification and commercialization activities relating to our products, which may change from time to time;
- the cost of manufacturing our products, which may vary depending on the quantity of production and the terms of our agreements with third-party suppliers and manufacturers; and
- future accounting pronouncements or changes in our accounting policies.

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

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

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

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

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

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

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

- delays or difficulties in enrolling patients in our clinical studies;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical studies, including the diversion of hospitals serving as our clinical study sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical study activities, such as clinical study site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical study subject visits and study procedures, the occurrence of which could affect the integrity of clinical study data;
- risk that participants enrolled in our clinical studies will contract the contagious disease while the clinical study is ongoing, which could impact the results of the clinical study, including by increasing the number of observed adverse events;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical studies, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- delays in receiving authorizations, allowances or approvals from local regulatory authorities to initiate our planned clinical studies;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical studies, including interruption in global shipping that may affect the transport of clinical study materials, such as investigational materials used in our clinical studies;
- changes in local regulations as part of a response to such pandemic or epidemic which may require us to change the ways in which our clinical studies are conducted, which may result in unexpected costs, or the discontinuation of such clinical studies altogether;
- interruptions or delays in preclinical studies due to restricted or limited operations at research and development laboratory facilities;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- refusal of the FDA to accept data from clinical studies in affected geographies.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Litigation and other legal proceedings may adversely affect our business.

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

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

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

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

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

- liabilities that substantially exceed our insurance levels, which we would then be required to pay from other sources, if available;
- an increase in our product liability insurance rates or the inability to renew or obtain product liability insurance coverage in the future on acceptable terms, or at all;
- withdrawal of clinical study volunteers or subjects;
- damage to our reputation and the reputation of our product candidates;
- regulatory investigations that could require costly recalls or product modifications;
- litigation costs; and
- diversion of our management's attention from managing our business.

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

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

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

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

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

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

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

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

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

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

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

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

In recent years, the global credit and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, inflation, declines in economic growth, wage inflation because of labor shortages and uncertainty about economic stability. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including the conflict between Russia and Ukraine and the conflict between the United States, Israel and Iran, terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also adversely impact the financial markets and the global economy, and any economic countermeasures by affected countries and others could exacerbate market and economic instability. In addition, the military conflict between the United States, Israel and Iran and escalation risks of a widening conflict in the Middle East are likely to continue to impact the global economy, and any prolonged or expanded conflict and instability in the Middle East could further disrupt global trade, energy supplies and market confidence. Each of the developments described above, or any combination of them, could adversely affect our businesses, financial condition and results of operations. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. These developments, or the perception that any of them could occur, may restrict the ability of key market participants to operate in certain financial markets or restrict our access to capital. For example, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our common stock.

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

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

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

The ability of the FDA, other government agencies and notified bodies to review and approve or certify new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's or other government agencies' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's, other government agencies' and notified bodies' ability to perform routine functions. These factors may also impact the FDA's ability to provide feedback on clinical trials and development programs, to meet with sponsors and to otherwise review regulatory submissions. Average review times at the FDA, other government agencies and notified bodies have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA, other agencies and notified bodies may also slow the time necessary for new drugs and medical devices or modifications to approved drugs or approved or certified medical devices to be reviewed and/or approved or certified by necessary government agencies or notified bodies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. In addition, the current U.S. presidential administration has sought to reduce the number of federal employees. If funding for the FDA is reduced, if the FDA workforce is reduced, if FDA priorities are changed or if a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions.

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

In addition, in the EU, notified bodies must be officially designated to certify products and services in accordance with the EU Medical Devices Regulation. While several notified bodies have been designated, currently designated notified bodies are facing a large amount of requests with the new regulation as a consequence of which review times have lengthened. This situation may impact the ability of our notified body(ies) to timely review and process our regulatory submissions, and our ability to grow our business in the EEA.

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

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

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

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

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

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

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

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

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

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

As of December 31, 2025, we had gross net operating loss ("NOL") carryforwards of approximately $205.4 million for federal income tax purposes, and $166.6 million for state income tax purposes, and approximately $8.8 million of federal research and development tax credits, after applying limitations under Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"). Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. Some of these NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We have experienced Section 382 ownership changes in the past, and the federal NOL disclosed above reflects the impact of the calculated Section 382 limitation. In addition, we may experience additional ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOLs is materially limited, it could harm our future operating results by effectively increasing our future tax obligations. In addition, under the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), future tax losses may be utilized to offset no more than 80% of the taxable income annually. There is also a risk that due to statutory or regulatory changes or other unforeseen reasons, our future NOLs could expire or otherwise be unavailable to offset future income tax liabilities. For these reasons, we may not be able to realize a tax benefit from the use of any future NOLs we generate, whether or not we attain profitability. As of December 31, 2025 and 2024, we recorded a full valuation allowance on these deferred tax assets. As of December 31, 2025, we had approximately $100.7 million of foreign net operating loss carryforwards related to our acquisition of Motus GI. Similarly, we have recorded a full valuation allowance on these deferred tax assets.

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

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

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

Risks Related to Our Reliance on Third Parties

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

We intend to primarily pursue licensing and distribution arrangements with strategic partners to commercialize and sell our product candidates. As such, licensing and collaboration payments, including upfront and milestone payments, as well as royalties and revenue sharing arrangements related to our products and product candidates, will account for substantially all of our revenue for the foreseeable future. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. We have limited experience in negotiating, establishing and managing such collaborations and we may be unable to successfully form and maintain such arrangements. For example, in 2025, we and Terumo entered into the Termination and ROFR Agreement, pursuant to which we and Terumo terminated the Terumo Agreement, and we may not be able to find a new strategic partner for our Virtue SAB product candidate. See *"Our Company—Our Flagship Candidates—Virtue SAB"* in Item (Business) of the Annual Report on Form 10-K.

Without commercialization partners, we may not have adequate financial or other resources to successfully commercialize our product candidates. In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for exclusive rights to commercialize our products or certain rights to control decisions regarding the development and commercialization of our products, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we have entered into or may enter into in the future, or any delay in entering into collaborations related to our products or product candidates, could delay the development and commercialization of our products or product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

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

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

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

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval, if any. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

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

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

We and our partners may be unable to sustain revenue growth.

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

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

Our medical device and component manufacturers must register with the FDA and are subject to periodic inspection by the FDA for compliance with the QMSR and cGMP, requirements, which require manufacturers of medical devices and drugs, respectively, to adhere to certain manufacturing practices, including design controls, product validation and verification, in process testing, quality control and documentation requirements. Similar requirements apply in foreign jurisdictions. Compliance with applicable regulatory requirements is subject to continual review and is rigorously monitored through periodic inspections or audits by the FDA and other regulatory agencies or notified bodies. Our component, polymer and drug suppliers are also required to meet certain standards applicable to their manufacturing processes.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The imposition of new duties, tariffs, trade barriers and retaliatory countermeasures implemented by the U.S. and other governments and the resulting impact on the cost of imported materials and demand for our future products may have a material adverse effect on our business, financial condition and results of operations.

The implementation of significant changes to U.S. trade policies, sanctions, legislation, treaties and tariffs, including, but not limited to, significant new tariffs on goods imported into the U.S., have introduced uncertainty to our business and may increase the cost of producing our product candidates for our clinical trials (and the cost of producing future products, if approved). In response, China announced and other countries have announced additional tariffs on U.S. goods. The imposition of additional tariffs or other trade barriers by countries outside of the U.S. may adversely affect our ability to market our future products (if approved) in these jurisdictions and increase our costs in these markets, which would adversely affect our financial results.

The extent and duration of increased tariffs and the resulting impact on general economic conditions and on our business are uncertain and depend on various factors, such as negotiations between the United States and affected countries, the responses of other countries or regions, exemptions or exclusions that may be granted, availability and cost of alternative sources of supply, and demand for our products in affected markets. United States and foreign policy changes and uncertainty about such changes have resulted in increased market volatility.

As a result of these dynamics, we may find it difficult to predict the impact to our business of these and future changes to the trading relationships between the U.S. or other countries or the impact on our business of new laws or regulations adopted by the United States or other countries.

Under recent legislation, certain third-party manufacturers and other third parties (frequently China-based companies) may be considered a "biotechnology company of concern." If a third-party manufacturer receives such a designation, it may restrict the ability of U.S. companies like us to purchase services or products from, collaborate with, or otherwise work with such manufacturers. For example, it may delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. Such disruption could have adverse effects on the development of our product candidates.

Risks Related to Government Regulation and Our Industry

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

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

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

Since its enactment, there have been judicial, U.S. Congressional and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. It is unclear how other healthcare reform measures of the new administration or other efforts, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, reduced Medicare payments to providers, effective on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 (the "MACRA"), enacted on April 16, 2015, repealed the formula by which Medicare made annual payment adjustments to physicians and implemented fixed annual updates and a new system of incentive payments that began in 2019 that are based on various performance measures and physicians' participation in alternative payment models such as accountable care organizations. In addition, the Inflation Reduction Act of 2022 included, among other things, provisions that impose new manufacturer financial liability on certain drugs under Medicare Part D, allowing the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition. It is unclear what effect new quality and payment programs, such as MACRA or the IRA, may have on our business, financial condition, results of operations or cash flows.

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

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

For instance, in December 2021, the EU Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. This regulation, which entered into force in January 2022, intends to boost cooperation among EU member states in assessing health technologies, including some medical devices, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies and making decisions on pricing and reimbursement.

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

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

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

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

We expect that obtaining regulatory approvals for our product candidates will require us to conduct human clinical studies. For our medical device product candidates and combination drug/device product candidates regulated as medical devices, we will need to obtain approval of an IDE, prior to beginning a clinical study in the United States. For our drug product candidates, we will need to submit an IND application that the FDA authorizes prior to beginning clinical studies in the United States. Preclinical studies, submissions related to CMC of our product candidates, and safety data such as biocompatibility will be required in connection with any IDE or IND applications. It is possible that unforeseen failure of one or more of these tests could cause delays in the application process.

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

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

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

Regulatory changes could result in restrictions on our ability to carry on or expand our operations, higher than anticipated costs or lower than anticipated sales. The FDA and foreign regulatory authorities enforce these regulatory requirements through various mechanisms, including periodic unannounced inspections. Failure to comply with applicable regulations could jeopardize our ability to sell our products and result in enforcement actions such as: warning letters; fines; injunctions; civil penalties; termination of distribution; recalls or seizures of products; delays in the introduction of products into the market; total or partial suspension of production; refusal to grant future approvals or certifications; withdrawals or suspensions of current approvals or certifications, resulting in prohibitions on sales of our products; and, in the most serious cases, criminal penalties.

Subject to the transitional provisions provided in the EU Medical Devices Regulation, and in order to sell our products in EU member states, our products must comply with the general safety and performance requirements of the EU Medical Devices Regulation, which repeals and replaces the Medical Devices Directive and the Active Implantable Medical Devices Directive. Compliance with these requirements is a prerequisite to be able to affix the CE mark to our products, without which they cannot be sold or marketed in the EU. All medical devices (including active implantable medical devices) placed on the market in the EU must meet the general safety and performance requirements laid down in Annex I to the EU Medical Devices Regulation, including the requirement that a medical device must be designed and manufactured in such a way that, during normal conditions of use, it is suitable for its intended purpose. Medical devices must be safe and effective and must not compromise the clinical condition or safety of patients, or the safety and health of users and — where applicable — other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. To demonstrate compliance with the general safety and performance requirements, we must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. A conformity assessment procedure generally requires the intervention of a notified body. The notified body would typically audit and examine the technical file and the quality system for the manufacture, design and final inspection of our devices. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EU. Failing to comply with applicable laws and regulations would preclude us from being able to affix the CE mark to our products, which would prevent us from selling them within the EU.

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

International regulatory approval or certification processes may take longer than the FDA approval process. We may be unable to obtain future regulatory approval or certification in a timely manner, or at all, especially if existing regulations are changed or new regulations are adopted. A failure or delay in obtaining necessary regulatory approvals or certifications would materially adversely affect our business.

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

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

The methods used in, and the facilities used for, the manufacture of our medical device products must comply with the FDA's QMSR which is a complex regulatory scheme that covers the procedures and documentation of the design, testing, production, process controls, quality assurance, labeling, packaging, handling, storage, distribution, installation, servicing and shipping of medical devices. Furthermore, we are required to verify that our suppliers maintain facilities, procedures and operations that comply with our quality standards and applicable regulatory requirements. The FDA enforces the QMSR through periodic announced or unannounced inspections of medical device manufacturing facilities, which may include the facilities of subcontractors. Our products are also subject to similar state regulations and various laws and regulations of foreign countries governing manufacturing. Our third-party manufacturers may not take the necessary steps to comply with applicable regulations, which could cause delays in the delivery of our products.

If any of these events occur, our reputation could be harmed, we could be exposed to product liability claims and we could lose customers and experience reduced sales and increased costs.

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

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

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

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

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

Moreover, the policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval or certification of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, with the change in U.S. presidential administrations in 2025, there continues to be substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates. If we experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired. In addition, the U.S. Supreme Court's June 2024 decision in Loper Bright Enterprises v. Raimondo overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rule-making process, any of which could adversely impact our business and operations. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval or certification that we may have obtained and we may not achieve or sustain profitability.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

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

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state and foreign laws that require drug and medical device manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information.

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

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

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

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

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

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

Demand for our products or new approved (or certified) indications for our existing products may fluctuate over time if federal, state and foreign legislative or administrative policy changes affect coverage or reimbursement levels for our products, or the services related to our products. In the United States, there have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system, some of which could have a material adverse effect on our business.

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

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

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

Even when HIPAA does not apply, according to the Federal Trade Commission (the "FTC"), failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. In 2024, the FTC finalized updates to the Health Breach Notification Rule that, among other things, clarified its applicability to health apps and other similar technologies and expanded the information the breach notification requirements for entities subject to the rule, which may add additional complexity to compliance obligations going forward.

In addition, certain state laws govern the privacy and security of health-related and other personal information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. By way of example, the California Consumer Privacy Act (the "CCPA"), which went into effect on January 1, 2020, gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, the California Privacy Rights Act (the "CPRA") passed in California in 2020, significantly amending the CCPA and imposing additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data and opt outs for certain uses of sensitive data. The CPRA also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have taken effect in Virginia, Colorado, Connecticut, Montana, Oregon, Texas, and Utah. Additionally, Delaware, Indiana, Iowa, Kentucky, Maryland, Minnesota, Nebraska, New Hampshire, New Jersey, Rhode Island and Tennessee have adopted privacy laws, which take effect from January 1, 2025 through 2026, reflecting a trend toward more stringent privacy legislation in the United States. In addition, some of these laws (including the CPRA), along with other standalone health privacy laws, subject health-related information to additional safeguards and disclosures and some specifically regulate consumer health data. For example, Washington's My Health My Data Act, effective as of March 31, 2024, imposes similar requirements specific to consumer health data. Similar laws have also passed in Connecticut and Nevada, which came into effect in 2023 and 2024. Further, numerous data privacy related legislative proposals remain pending at the federal level as well. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

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

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

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

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

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

Federal, state, local and foreign laws regarding environmental protection, hazardous substances and human health and safety may adversely affect our business. Using hazardous substances in our operations exposes us to the risk of accidental injury, contamination or other liability from the use, storage, importation, handling or disposal of hazardous materials. If our or our suppliers' operations result in the contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and fines, and any liability could significantly exceed our insurance coverage and have a material adverse effect on our business, financial condition, results of operations and prospects. Future changes to environmental and health and safety laws could cause us to incur additional expenses or restrict our operations.

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights if patent rights are awarded to third parties instead of to us. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications. Such challenges may result in loss of patent rights, in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology or products. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could have a material adverse effect on our business, financial condition and results of operations.

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

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

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We may intentionally choose not to or inadvertently fail to comply with such requirements. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in the abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition and results of operations.

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

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act"), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application at the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to file any patent application related to our products or invent any of the inventions claimed in our patents or patent applications.

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

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

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

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

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

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

In the United States, a patent that covers a medical device approved by the FDA may be eligible for a term extension designed to restore the period of the patent term that is lost during the pre-market regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our products, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the EU, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

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

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

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

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

Risks Related to Ownership of Our Common Stock

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

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

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

Certain provisions of Delaware law, as well as provisions in our certificate of incorporation ("Charter") and our bylaws ("Bylaws"), may discourage unsolicited takeover proposals that stockholders may consider to be in their best interests. These provisions may make it more difficult to remove management and may discourage transactions that otherwise could involve payment of a premium over prevailing market prices for our securities. Among other things, these provisions:

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

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

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

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

This exclusive forum provision would not apply to suits brought to enforce a duty or liability vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, such as those created by the Exchange Act or the Securities Act of 1933, as amended (the "Securities Act"), or any other claim for which the federal courts have exclusive jurisdiction. In addition, to prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our Charter provides that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. However, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, both state and federal courts have jurisdiction to entertain such claims. As noted above, our Charter provides that the federal district courts of the United States will be the exclusive forum for the resolution of any complaint asserting a cause of action under the Securities Act. Due to the concurrent jurisdiction for federal and state courts created by Section 22 of the Securities Act over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder, there is uncertainty as to whether a court would enforce the exclusive forum provision. Our Charter further provides that any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and to have consented to these provisions. Investors also cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

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

The price of our common stock has in the past been volatile and may continue to be volatile and subject to significant fluctuation.

Fluctuations in the price of our securities could contribute to the loss of all or part of your investment. The trading price of our common stock has experienced volatility. For example, from January 1, 2025 through March 12, 2026, the closing price of our common stock on the Nasdaq Global Stock Market ranged from a high of $5.98 to a low of $2.35. The price of our common stock may continue to experience volatility in the future and is subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of such factors, including the factors listed below, could have a material adverse effect on your investment in our securities and our securities may trade at prices significantly below the price you paid. In such circumstances, the trading price of our securities may not recover and may experience a further decline.

Factors affecting the trading price of our securities may include:

- the results of our clinical trials;
- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- changes in the market's expectations about our operating results;
- the inability to maintain our listing on Nasdaq;
- our operating results failing to meet the expectation of securities analysts or investors in a particular period;
- changes in financial estimates and recommendations by securities analysts concerning us or the market in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- our ability to develop product candidates;
- changes in laws and regulations affecting our business;
- litigation involving us;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of our securities available for public sale;
- any major change in our Board or management;
- sales of our securities by directors, executive officers or significant stockholders, or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

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

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

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

We cannot be certain when or if our operations will generate sufficient cash to fund our ongoing operations or the growth of our business. We intend to make investments to support our current business and may require additional funds to respond to business challenges. Additional financing may not be available on favorable terms, if at all. If adequate funds are not available on acceptable terms, we may be unable to invest in our future growth opportunities, which could harm our business, operating results and financial condition. If we incur debt, the debt holders could have rights senior to holders of our common stock to make claims on our assets. The terms of any debt could restrict our operations, including our ability to pay dividends on our common stock. If we issue additional equity securities in the future, our stockholders will experience dilution, and the new equity securities could have rights senior to those of our common stock. For example, in connection with the Termination and ROFR Agreement, Terumo purchased Series A Preferred Stock, which is convertible into common stock in the future, subject to certain conditions, at a minimum of $12 per share. The Series A Preferred Stock has preference to our common stock with respect to, among other things, payment upon liquidation of the Company. Because the decision to issue additional securities in the future will depend on numerous considerations, including factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future issuances of debt or equity securities. As a result, stockholders will bear the risk of future issuances of debt or equity securities reducing the value of their common stock and diluting their interest.

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

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

The holders of an aggregate of up to 17,148,494 shares of common stock (not including 1,310,000 shares underlying warrants) or approximately 29% of our outstanding common stock as of March 10, 2026, are entitled to registration rights under the Second Amended and Restated Registration Rights Agreement and Lock-Up Agreement, as of November 21, 2023 (the "Amended and Restated Registration Rights Agreement") entered into in connection with the closing of the Business Combination, and the Company has registered, among other things, the resale of those outstanding shares of Common Stock as well as the issuance of shares of Common Stock underlying warrants. In certain circumstances, holders of these securities can demand that we conduct an underwritten offering of their securities or facilitate block trades of their securities. In addition, the holders have certain "piggy-back" registration rights with respect to registration statements we file. We will bear the expenses incurred in connection with the filing of any such registration statements. The presence of these additional shares trading in the public market may have an adverse effect on the market price of our securities.

Due to the significant number of redemptions of HSAC2's ordinary shares in connection with the Business Combination, there was a significantly lower number of HSAC2 ordinary shares that converted into shares of our common stock in connection with the Business Combination. As a result, the shares of our common stock being registered for resale constitute a considerable percentage of our public float. Additionally, some of the shares of our common stock being registered for resale were originally purchased by selling securityholders pursuant to investments in Orchestra BioMed, Inc. at prices considerably below the current market price of our common stock. This discrepancy in purchase prices may have an impact on the market perception of our common stock's value and could increase the volatility of the market price of our common stock or result in a significant decline in the public trading price of our common stock. The registration of these shares for resale creates the possibility of a significant increase in the supply of our common stock in the market. The increased supply, coupled with the potential disparity in purchase prices, may lead to heightened selling pressure, which could negatively affect the public trading price of our common stock.

Our warrants may not be exercised at all and we may not receive any cash proceeds from the exercise of the warrants.

The exercise prices of our warrants, in certain circumstances, may be higher than the prevailing market price of our underlying common stock and the cash proceeds to us associated with the exercise of our warrants are contingent upon our stock price. The value of our common stock may fluctuate and may not exceed the exercise price of the warrants at any given time. As of the date of this Annual Report on Form 10-K, a significant portion of our warrants are "out of the money," meaning the exercise price is higher than the market price of our common stock. Holders of such "out of the money" warrants are not likely to exercise such warrants. There can be no assurance that such warrants will be in the money prior to their respective expiration dates, and therefore, we may not receive any cash proceeds from the exercise of such warrants. See *"Management's Discussion and Analysis of Financial Condition and Results of Operations – Liquidity and Capital Resources" for additional information."*

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.

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

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

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

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

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

We are a smaller reporting company and the reduced reporting requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We no longer qualify as an "emerging growth company" as defined in Section 2(a)(19) of the Securities Act, as modified by the JOBS Act. However, for so long as we qualify as a "smaller reporting company," we will have the option to take advantage of certain exemptions from various reporting and other requirements that are applicable to other public companies that are not "smaller reporting companies," including but not limited to reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and later effective dates for compliance with certain new disclosure obligations. We will remain a smaller reporting company if we have either (i) a public float of less than $250.0 million held by non-affiliates as of the last business day of the second quarter of our then-current fiscal year or (ii) annual revenues of less than $100.0 million during such recently completed fiscal year with less than $700.0 million in public float as of the last business day of the second quarter of such fiscal year.

In addition, we will not be required to include an attestation report of our registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act') due to an exemption for certain "smaller reporting companies. We will continue to not be required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act as long as (a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting common stock held by non-affiliates is less than $700.0 million as of the last business day of the second quarter of such fiscal year.

We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile and may decline.

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

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

If we are unable to assess whether our internal control over financial reporting is effective, we may be subject us to adverse regulatory consequences, a loss of investor confidence and a decrease in the market price of our common stock. If we are unable to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, we could become subject to investigations by Nasdaq, the SEC or other regulatory authorities, which could require additional financial and management resources.

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

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

There are significant financial costs and expenses for complying with the Sarbanes-Oxley Act, including the requirements of Section 404, as well as rules and regulations of the SEC, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the rules and regulations thereunder, rules and regulations of the Public Company Accounting Oversight Board ("PCAOB") and Nasdaq. Compliance with public company requirements increases costs and requires the expenditure of significant managements resources. Advocacy efforts by stockholders and third parties may also prompt additional changes in governance and reporting requirements, which could further increase costs and administrative burdens. In order to comply with these requirements, we carry out activities that Orchestra BioMed, Inc. had not done previously. For example, since becoming a public company, we have created and adopted internal controls and disclosure controls and procedures, all of which have increased expenses and administrative burdens. In addition, we have new expenses associated with SEC reporting requirements.

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

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

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

Item 1B. Unresolved Staff Comments

Not Applicable.

Item 1C. Cybersecurity

Orchestra BioMed, ("Orchestra" or "Company") maintains a cyber risk management program designed to identify, assess, manage, mitigate, and respond to cybersecurity threats. This program, in conjunction with the Company's enterprise risk management assessment processes, addresses cybersecurity risks to the corporate information technology environment including systems, hardware, software, data, people, and processes.

Cybersecurity Risk Management

The underlying processes and controls of cyber risk management program incorporate recognized best practices and standards for cybersecurity and information technology, including the National Institute of Standards and Technology ("NIST") Cybersecurity Framework ("CSF"). Orchestra has an annual assessment performed by a third-party specialist of the Company's cyber risk management program against the NIST CSF. The annual risk assessment identifies, quantifies, and categorizes material cyber risks. In addition, the Company, in conjunction with the third-party cyber risk management specialists, develops a risk mitigation plan to address such risks, and where necessary, remediate potential vulnerabilities identified through the annual assessment process.

In addition, Orchestra maintains policies over areas such as information security, IT change and configuration management, acceptable use, access on/offboarding, and data backup and recovery to help govern the processes put in place by management designed to protect Orchestra's IT assets, data, and services from threats and vulnerabilities. Orchestra partners with industry recognized cybersecurity providers leveraging third-party technology and expertise. Cybersecurity partners to the Company, including consultants and other third-party service providers, are a key part of Orchestra's cybersecurity risk management strategy and infrastructure and provide services including maintenance of an IT assets inventory, periodic vulnerability testing, identity access management controls, including restricted access of privileged accounts, physical security measures at Company facilities, information protection/detection systems including maintenance of firewalls and anti-malware tools, network and traffic monitoring and automated alerting, ongoing cybersecurity user awareness training, remote monitoring and management, capacity management, industry-standard encryption protocols, formalized processes over asset and data destruction, formalized change management processes, data backups management, infrastructure maintenance, incident response, cybersecurity strategy, and cyber risk advisory, and assessment. In the event of an incident, the Cyber Risk Committee would be notified and appropriate action would be taken to resolve the incident, including notifying senior management and, as appropriate, our Board.

Orchestra has implemented third-party risk management processes to manage the risks associated with reliance on vendors, critical service providers, and other third-parties that may lead to a service disruption or an adverse cybersecurity incident. This includes assessment of vendors during the selection/onboarding process, internal controls and security standards of vendors, compliance with service level agreements, review of System & Organization Controls (SOC) reports on an annual basis and a regular review of vendor contracts.

Governance

Orchestra's Cyber Risk Committee, in conjunction with third-party IT and cybersecurity service providers is responsible for oversight and administration of Orchestra's cyber risk management program, and for informing senior management, our Board, and other relevant stakeholders regarding the prevention, detection, mitigation, and remediation of cybersecurity incidents. The Company's management team has prior experience selecting, deploying, and overseeing cybersecurity technologies, initiatives, and processes via selection of strategic third-party partners (such as the Company's virtual Chief Information Security Officer), and relies on threat intelligence as well as other information obtained from governmental, public, or private sources, including external consultants engaged by Orchestra for strategic cyber risk management, advisory and decision making.

The Audit Committee of our Board of Directors oversees Orchestra's cybersecurity risk exposures and the steps taken by management to monitor and mitigate cybersecurity risks. Members of the Cyber Risk Committee brief the Audit Committee on cyber vulnerabilities identified through the risk management process, the effectiveness of Orchestra's cyber risk management program, and the emerging threat landscape and new cyber risks on at least an annual basis. This includes reporting cybersecurity incidents and updates on Orchestra's processes to prevent, detect, and mitigate cybersecurity incidents. In addition, cybersecurity risks are reviewed by our Board, at least annually, as part of the Company's corporate risk oversight processes.

Orchestra faces risks from cybersecurity threats that could have a material adverse effect on its business, financial condition, results of operations, cash flows or reputation. Orchestra acknowledges that the risk of cyber incident is prevalent in the current threat landscape and that a future cyber incident may occur in the normal course of its business. However, prior cybersecurity incidents have not had a material adverse effect on Orchestra's business, financial condition, results of operations, or cash flows. The Company proactively seeks to detect and investigate unauthorized attempts and attacks against IT assets, data, and services, and to prevent their occurrence and recurrence where practicable through changes or updates to internal processes and tools and changes or updates to the Company's service delivery; however, potential vulnerabilities to known or unknown threats will remain. Further, there is increasing regulation regarding responses to cybersecurity incidents, including reporting to regulators, investors, and additional stakeholders, which could subject the Company to additional liability and reputational harm. In response to such risks, the Company has implemented initiatives such as implementation of the cybersecurity risk assessment process and development of an incident response plan. See *"Our information technology systems, or those of any of our CROs, manufacturers, other contractors, consultants, collaborators or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations" in Item 1A (Risk Factors)* for more information on cybersecurity risks.

Item 2. Properties

Our headquarters are located at 150 Union Square Drive New Hope, Pennsylvania 18938, where we lease 8,052 rentable square feet of office and laboratory space under a lease that terminates on September 30, 2027. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we may become involved in various claims and legal proceedings that arise in the ordinary course of our business. We are not currently a party to any material legal proceedings and are not aware of any pending or threatened legal proceeding against us that we believe would have a material adverse effect on our business, operating results or financial condition.

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

Item 5. Market for Registrant's Company Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is currently listed on the Nasdaq Global Market under the symbol "OBIO".

Holders

As of March 10, 2026, there were 715 holders of record of our common stock, which amount does not include participants of The Depository Trust Company or beneficial owners holding shares through nominee names.

Dividend Policy

We have not paid any cash dividends on our common stock to date. We anticipate that we will retain all of our future earnings, if any, for the development, operation and expansion of our business and we do not anticipate declaring or paying any cash dividends for the foreseeable future. Any future determination to pay dividends will be made at the discretion of our Board, subject to applicable laws. Such determination will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual, legal, tax and regulatory restrictions, general business conditions, and other factors that our Board may deem relevant. Should we decide in the future to do so, as a holding company, our ability to pay dividends on our capital stock and meet other obligations depends upon the receipt of dividends or other payments from our operating subsidiaries, including Orchestra BioMed, Inc. In addition, the payment of cash dividends is prohibited by the terms of the 2024 LSA and the Medtronic Loan Agreement, and any future debt financing arrangement likely will also contain terms restricting or limiting the amount of dividends that may be declared or paid on our securities.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans in Item 12 of Part III of this Annual Report on Form 10-K is incorporated herein by reference.

Recent Sales of Unregistered Securities

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Unless otherwise indicated or the context otherwise requires, references to "Orchestra," "Orchestra's," "the Company," "we," "its" and "our" refer to Orchestra BioMed Holdings, Inc. and its consolidated subsidiaries. All references to years, unless otherwise noted, refer to the Company's fiscal years, which end on December 31.

The following discussion should be read together with "Special Note Regarding Forward-Looking Statements" and the Company's audited consolidated financial statements, together with the related notes thereto, included in Item 8 of this Annual Report on Form 10-K (the "Consolidated Financial Statements"). In addition to historical financial information, this discussion contains forward-looking statements based upon our current expectations that involve risks and uncertainties. Our actual results could differ materially from such forward-looking statements as a result of various factors, including those set forth under "Item 1A. Risk Factors" herein.

Overview

We are a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. Our partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products we develop. We are led by a highly accomplished, multidisciplinary management team and a board of directors with extensive experience in all phases of therapeutic device development. Our business was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by our founding team.

Our flagship product candidates are Atrioventricular Interval Modulation Therapy ("AVIM Therapy") for the treatment of hypertension ("HTN"), the leading risk factor for death worldwide, and Virtue® Sirolimus AngioInfusion™ Balloon ("Virtue SAB") for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. We have an exclusive license and collaboration agreement with Medtronic Inc. (an affiliate of Medtronic plc) ("Medtronic") for the development and commercialization of AVIM Therapy for the treatment of uncontrolled HTN in patients indicated for a cardiac pacemaker (as amended, the "Medtronic Agreement"). We are actively conducting a double-blind, randomized, global pivotal study (the "BACKBEAT study"), enrolling up to 500 patients with uncontrolled hypertension who are indicated for a Medtronic dual-chamber pacemaker, with enrollment completion currently planned for mid-2026. We recently initiated patient enrollments in the Virtue SAB in the Treatment of Coronary In-Stent Restenosis ("ISR") Trial (the "Virtue Trial") for our U.S. investigational device exemption ("IDE") pivotal study randomizing Virtue SAB vs. Boston Scientific Corporation's AGENT™ drug-coated balloon. Designed to support regulatory approval of Virtue SAB, the Virtue Trial is expected to enroll 740 patients in the United States with enrollment completion currently planned for mid-2027. We cannot provide assurance that we will be able to complete enrollment of the BACKBEAT study or the Virtue Trial in the timeframes we anticipate.

Since Orchestra BioMed, Inc.'s inception, we have devoted the substantial majority of our resources to performing research and development and clinical activities in support of our product development and collaboration efforts. We have funded our operations primarily through the issuance of common stock, convertible preferred stock, and warrants, as well as proceeds from the Business Combination, our prior Terumo Agreement and the Termination and ROFR Agreement, borrowings under debt arrangements, the sale of future revenues, and, to a lesser extent, from product revenue from our subsidiary, FreeHold Surgical, LLC. ("FreeHold"). As of December 31, 2025, we have raised a cumulative $356.5 million in gross proceeds. Future committed cash receipts expected in April 2026 include $20.0 million from the Medtronic Loan Agreement (as such term is defined in Note 16 to the Consolidated Financial Statements – *"Debt Financing"*), and an additional $15.0 million from Ligand pursuant to the Royalty Purchase Agreement. On January 9, 2026, we received $4.7 million pursuant to the sale of our Vivasure investment. We have incurred net losses each year since inception. Our net losses were $52.7 million and $61.0 million for the years ended December 31, 2025 and 2024, respectively. We expect to continue to incur significant losses for the foreseeable future. As of December 31, 2025, we had an accumulated deficit of $362.6 million.

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

Recent Developments

On January 9, 2026, Haemonetics Corporation ("Haemonetics"), a global medical technology company focused on delivering innovative solutions designed to improve patient outcomes, announced its acquisition of Vivasure Medical Limited ("Vivasure"), a Galway, Ireland-based company pioneering next-generation technology for percutaneous vessel closure. Vivasure was a strategic holding of ours prior to its acquisition. In connection with the closing of the transaction, we can receive up to $10.7 million of proceeds in 2026 associated with the transaction. In January, we received the initial upfront payment of $4.7 million and the remainder may be received in 2026 based on the achievement of a milestone. We may receive additional proceeds in the future associated with revenue earnouts based on the achievement of certain milestones.

Components of Our Results of Operations

Partnership Revenue

To date, our partnership revenues have related to the Terumo Agreement described below. In future periods, partnership revenues may also include revenues related to the Exclusive License and Collaboration Agreement, dated as of September 30, 2022, by and among, Orchestra BioMed, Inc., BackBeat Medical, LLC and Medtronic, discussed in Note 4 to the Consolidated Financial Statements.

Orchestra BioMed, Inc. entered into the Terumo Agreement in June 2019 and has determined that the arrangement represents a contract with a customer and is therefore in scope of ASC 606, *Revenues from Contracts with Customers* ("ASC 606"). Under the Terumo Agreement, Orchestra BioMed, Inc. received an upfront payment of $30.0 million in 2019 and an equity commitment of up to $5.0 million of which $2.5 million was invested in June 2019 as part of the Orchestra BioMed, Inc. Series B-1 financing and $2.5 million was invested in June 2022 as part of the Orchestra BioMed, Inc. Series D-2 financing.

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

On October 28, 2025, we entered into a termination and right of first refusal agreement (the "Termination and ROFR Agreement") with Terumo with respect to Virtue SAB. The Termination and ROFR Agreement, which supersedes and terminates the Terumo Agreement, grants Terumo a right of first refusal ("ROFR") to acquire the rights, or enter a distribution arrangement, with respect to Virtue SAB for the treatment of coronary artery disease, in exchange for an upfront payment of $10.0 million. In connection with the Termination and ROFR Agreement, on November 7, 2025, Terumo invested an additional $20.0 million in Orchestra BioMed through our Series A Preferred Stock, which is convertible into common stock in the future, subject to certain conditions, at a minimum of $12 per share. Pursuant to the terms of the Termination and ROFR Agreement, Orchestra BioMed, Inc. has no further performance obligations under the Terumo Agreement and therefore recognized the remaining amounts of deferred revenue. We recognized $30.0 million in cumulative partnership revenues from 2019 through December 31, 2025. In addition to recognizing the remainder of the deferred revenue, partnership revenue for the year ended December 31, 2025 included $10.0 million in consideration for the ROFR and $7.4 million associated with the premium above the fair market value of the Series A Preferred Stock.

In June 2022, Orchestra BioMed, Inc. entered into the Medtronic Agreement for the development and commercialization of AVIM Therapy for the treatment of pacemaker-indicated patients with uncontrolled HTN despite the use of anti-hypertensive medications. On July 31, 2025, Orchestra BioMed, Inc., our wholly owned subsidiary BackBeat Medical, LLC, and Medtronic entered into an amendment to the Medtronic Agreement, which became effective on August 4, 2025 (the "Medtronic Agreement Amendment"), to provide, among other things, a development and commercialization framework for future AVIM-therapy integration into a dual-chamber leadless pacemaker. Pursuant to the Medtronic Agreement Amendment, we will be required, among other things, to reimburse Medtronic for certain expenses incurred in connection with the integration of AVIM-therapy into Medtronic's dual-chamber leadless pacemaker, up to a specified cap.

We have determined that the arrangement is a collaboration within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808"). In addition, we concluded that Medtronic is a customer for a good or service that is a distinct unit of account, and therefore, the transactions in the Medtronic Agreement, as amended pursuant to the Medtronic Agreement Amendment (the "Amended Medtronic Agreement"), should be accounted for under ASC 606. Through December 31, 2025, there have been no amounts recognized as revenue under the Amended Medtronic Agreement.

Product Revenue

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

Cost of Product Revenue and Gross Margin

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

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

Research and Development Expenses

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

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

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

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist of personnel-related expenses, including salaries, benefits, bonus, travel and stock-based compensation. Other selling, general and administrative expenses include professional services fees, including legal, audit investor/public relations, and insurance costs, outside consultants costs, employee recruiting and training costs, and non-income taxes. Moreover, we incur and expect to continue to incur additional expenses associated with operating as a public company, including legal, accounting, insurance, exchange listing and U.S. Securities and Exchange Commission ("SEC") compliance, and investor relations expenses. We expect annual selling, general and administrative expenses to continue to increase as we conduct additional clinical trials and expand our operations as a public company.

Interest (Expense) Income, Net

Interest (expense) income, net reflects the income generated from marketable securities during the year. Interest expense is attributable to loan interest and interest related to the Royalty Purchase Agreement.

On July 31, 2025, we entered into a revenue participation right purchase and sale agreement (the "Royalty Purchase Agreement") with Ligand Pharmaceuticals Incorporated ("Ligand"). Under the terms of the Royalty Purchase Agreement, in exchange for payment of $35.0 million (the "Investment Amount"), less certain reimbursable expenses, Ligand acquired the right to receive tiered royalty payments from us (the "Royalty Interest") with respect to revenue (including certain licensing revenue) received by us in a calendar year in connection with worldwide net product sales, or other product revenue received by, by us and our licensees ("Annual Net Sales") of (a) AVIM Therapy (the "Primary Product") and (b) Virtue SAB (the "Secondary Product" and together with the Primary Product, the "Products") in the field of coronary artery treatment. At execution of the Royalty Purchase Agreement, our estimate of this total interest expense resulted in an effective annual interest rate of approximately 23.1%. This estimate contains significant assumptions that impact both the amount recorded at execution and the interest expense that will be recognized over the royalty period. We will periodically assess the estimated amounts due and payable to Ligand and to the extent the amount or timing of such payments is materially different than the original estimates, an adjustment will be recorded prospectively to increase or decrease interest expense. There are a number of factors that could materially affect the amount and timing of the royalty payments to be paid by us to Ligand and, correspondingly, the amount of interest expense recorded by us.

On November 6, 2024 (the "LSA Closing Date"), we and certain of our subsidiaries (collectively, the "Borrower") entered into a Loan and Security Agreement, by and among the Borrower, the several banks and other financial institutions or entities party thereto, as lenders (collectively, the "Hercules Lenders"), and Hercules Capital, Inc. ("Hercules"), as administrative agent and collateral agent for itself and the Hercules Lenders, as amended by that certain First Amendment to Loan and Security Agreement dated as of December 30, 2024 ("2024 LSA"). Prior to July 31, 2025, the 2024 LSA provided a secured term loan facility of up to $50.0 million available in up to four tranches (collectively, the "Term Loans"), with the first tranche of $15.0 million drawn on the LSA Closing Date, and a second and third tranche of up to an aggregate of $15.0 million available upon achievement of certain performance and financing milestones. Additionally, we had access to a fourth tranche of $20.0 million subject to future approval. On July 31, 2025, the Borrower, the Hercules Lenders and Hercules entered into the Second Amendment to the 2024 LSA, which, amended the 2024 LSA to, among other things, (i) delay the initial date upon which we must begin amortizing term loans under the 2024 LSA from (a) December 1, 2026 (with amortization payments delayed to as late December 1, 2027 if certain conditions were met) to (b) July 1, 2027 (with amortization payments delayed to as late as January 1, 2028 if certain conditions are met); (ii) increase by $15.0 million (from $20.0 million to $35.0 million) the amount that that may be borrowed by us in the discretion of the lender's investment committee's and (iii) eliminate our ability to draw up to $15.0 million if certain milestones are achieved. The Term Loan has a maturity date of November 6, 2028 and accrues interest at a floating per annum rate equal to the greater of (i) (x) the "prime rate" as reported in The Wall Street Journal plus (y) 2.0%, and (ii) 9.50%. Refer to Note 16 – *"Debt Financing"* to our Consolidated Financial Statements.

Change in the fair value of derivative liability

In November 2025, we sold 200,000 shares of Series A Preferred Stock at a purchase price equal to $100.00 per share for gross proceeds of $20.0 million. We concluded that certain conversion and redemption features meet the requirements to be separately accounted for as a bifurcated derivative. As a result, we bifurcated the Series A Preferred Stock between (i) the host contract, which was accounted for within mezzanine equity, and (ii) the bifurcated derivative liabilities related to those conversion and redemption features. The bifurcated derivatives are remeasured to fair value at each reporting period with changes in fair value recorded in the consolidated statement of operations and comprehensive loss.

Loss on Fair Value of Strategic Investments

The loss on fair value of strategic investments represents a change in the fair value of our investment in common stock holdings of a previously publicly-held company. The common stock held represented equity securities with a readily determinable fair value and were required to be measured at fair value at each reporting period using readily determinable pricing available on a securities exchange, in accordance with the provisions of ASU 2016-01.

Results of Operations

Comparison of the Years Ended December 31, 2025 and 2024

The following table presents our statement of operations data for the years ended December 31, 2025 and 2024, and the dollar and percentage change between the two periods (in thousands):

	Year Ended December 31,			
	2025	2024	Change $	Change %
Revenue:				
Partnership revenue	$ 32,871	$ 2,005	$ 30,866	1,539 %
Product revenue	611	633	(22)	(3)%
Total revenue	33,482	2,638	30,844	1,169 %
Expenses:				
Cost of product revenues	190	204	(14)	(7)%
Research and development	58,185	42,804	15,381	36 %
Selling, general and administrative	26,914	23,931	2,983	12 %
Total expenses	85,289	66,939	18,350	27 %
Loss from operations	(51,807)	(64,301)	12,494	19 %
Other (expense) income:				
Interest (expense) income, net	(1,148)	3,356	(4,504)	(134)%
Change in the fair value of derivative liability	254	—	254	100 %
Loss on fair value of strategic investments	—	(68)	68	100 %
Other expense	—	(11)	11	100 %
Total other (expense) income	(894)	3,277	(4,171)	(127)%
Net loss	$ (52,701)	$ (61,024)	$ 8,323	14 %

Partnership Revenue

Partnership revenue increased by $30.9 million, or approximately 1539%, to $32.9 million in the year ended December 31, 2025 from $2.0 million for the year ended December 31, 2024. Partnership revenue relates partially to the recognition of the combined performance obligation for the license granted to Terumo and the ongoing research and development services over the estimated performance period for the Virtue SAB coronary ISR indication, using a proportional performance model, based on the costs incurred relative to the total estimated costs of the research and development services. Partnership revenue primarily relates to our entering into the Termination and ROFR Agreement with Terumo on October 28, 2025, for which we received $30.0 million in exchange for providing a ROFR and issuing Series A Preferred Stock to Terumo. The Termination and ROFR Agreement superseded and terminated the Terumo Agreement, and we no longer have any performance obligations under the Terumo Agreement. In addition to recognizing the remainder of the deferred revenue, partnership revenue for the year ended December 31, 2025 included $10.0 million in consideration for the ROFR and $7.4 million associated with the premium above the fair market value of the Series A Preferred Stock.

Prior to the termination of the Terumo Agreement, as of each quarterly reporting date, we evaluated our estimates of the total costs expected to be incurred through the completion of the combined performance obligation and updated our estimates as necessary. For the year ended December, 31, 2025, the termination of the Terumo Agreement resulted in the conclusion of the related performance obligations and therefore, resulted in the recognition of the remaining deferred revenue. For the year ended December 31, 2024, the expenses incurred related to the Terumo Agreement were $12.5 million. The estimated total costs associated with the Terumo Agreement through completion increased by approximately 5.0% as of December 31, 2024, as compared to the estimates as of December 31, 2023.

Product Revenue

Product revenue decreased by $22,000, or approximately 3%, to $611,000 in the year ended December 31, 2025 from $633,000 for the year ended December 31, 2024.

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

Cost of Product Revenue

Cost of product revenue decreased by $14,000, or approximately 7%, to $190,000 in the year ended December 31, 2025 from $204,000 for the year ended December 31, 2024. The decrease was primarily due to lower sales volume of FreeHold Duo and Trio intracorporeal organ retractors.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2025 and 2024 (in thousands):

	Year Ended December 31,	
	2025	2024
Personnel and consulting costs	$ 26,974	$ 19,278
Non-clinical development costs	18,266	15,447
Clinical development costs	12,945	8,079
Total research and development expenses	**$ 58,185**	**$ 42,804**

Research and development expenses increased by $15.4 million, or approximately 36%, to $58.2 million for the year ended December 31, 2025 from $42.8 million for the year ended December 31, 2024. This is primarily due to an increase in support of ongoing work to advance the BACKBEAT study and to advance Virtue SAB into the Virtue Trial, which commenced in October 2025. The increase included an increase of $4.9 million in clinical development costs, an increase in personnel-related expenses of $6.6 million due to increased headcount and consulting costs, an increase of $2.8 million in non-clinical development costs associated with research and development program costs, supplies, and testing, and an increase in stock-based compensation of $1.1 million.

The total research and development expenses summarized above include $14.3 million for the year ended December 31, 2025 and $12.3 million for the year ended December 31, 2024 related to the Terumo Agreement. The increase of $2.0 million is due to increased expense activity related to the Terumo Agreement during the 2025 period.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $3.0 million, or approximately 12%, to $26.9 million for the year ended December 31, 2025, from $23.9 million of expense for the year ended December 31, 2024. The increase primarily resulted from an increase of $1.9 million in accounting, finance, legal, marketing, investor relations and public relations expenses, an increase in personnel-related expenses of $871,000 due to increased headcount and consulting costs, and an increase of $220,000 in stock-based compensation.

Interest (Expense) Income, Net

Interest (expense) income, net, decreased by $4.5 million, or approximately 134%, to $1.1 million of expense for the year ended December 31, 2025 from $3.4 million of income for the year ended December 31, 2024. The net interest expense in the 2025 period consisted primarily of monthly interest expense resulting from the 2024 LSA and the Royalty Purchase Agreement partially offset by interest earned from marketable securities. The net interest income in the 2024 period consisted primarily of interest earned from marketable securities. The decrease in interest (expense) income, net resulted from interest expense related to the Royalty Purchase Agreement, which was not in place during 2024.

Change in the fair value of derivative liability

The derivative liability of the Series A Preferred Stock was remeasured to a fair value of $2.7 million as of December 31, 2025. We recognized a gain of $254,000 for the year ended December 31, 2025, primarily driven by decreases in our stock price compared to initial measurement at issuance.

Loss on Fair Value of Strategic Investments

No gain or loss on fair value of strategic investments was recognized for the year ended December 31, 2025 as compared to a loss of $68,000 for the year ended December 31, 2024 related to the change in fair value in our common stock holdings of a previously publicly-held company.

Liquidity and Capital Resources

Overview

From inception through December 31, 2025, we have incurred significant operating losses and negative cash flows from our operations. Our net losses were $52.7 million and $61.0 million for the years ended December 31, 2025 and December 31, 2024, respectively. As of December 31, 2025, we had an accumulated deficit of $362.6 million. We have funded our operations primarily through the issuance of common stock, convertible preferred stock, and warrants, as well as proceeds from the Business Combination, the prior Terumo Agreement and the ROFR and Termination Agreement, borrowings under debt arrangements, the sale of future revenues, and to a lesser extent, revenue from FreeHold products. As of December 31, 2025, we have raised a cumulative total of $356.5 million in gross proceeds. We had $106.5 million in cash and cash equivalents and marketable securities at December 31, 2025, comprised of $34.7 million in cash and cash equivalents and $71.8 million in marketable securities. Cash and cash equivalents consisted primarily of bank deposits and money market funds while short-term marketable securities consisted primarily of our investments in corporate debt securities. Future committed cash receipts expected in April 2026 include $20.0 million from the Medtronic Loan Agreement, and an additional $15.0 million from Ligand pursuant to the Royalty Purchase Agreement. On January 9, 2026, Haemonetics closed on an acquisition of Vivasure in which we can receive up to $10.7 million of proceeds in 2026 made up of approximately $4.7 million upfront and approximately $6.0 million in a first milestone payment.

Funding Requirements

We intend to prioritize spending on our two flagship product candidates and expect operating expenses to increase accordingly as we focus on continued execution of the BACKBEAT study for AVIM Therapy and ramp up execution of the recently initiated Virtue Trial for Virtue SAB. The additional investment will primarily support clinical study costs as well as other research and development activities.

Based on internally prepared budget estimates that reflect our operating priorities, we anticipate that our Cash and cash equivalents, Marketable securities, proceeds received subsequent to December 31, 2025 but prior to the filing of this Annual Report on Form 10-K, expected future proceeds from contractual financing commitments and other potential future proceeds described below are sufficient to fund our operations into the fourth quarter of 2027. The amount and timing of our future funding requirements may change from this current estimate and are dependent on many factors, including the cost and pace of execution of clinical studies and research and development activities, the strength of results from clinical studies and other research, development and manufacturing efforts, as well as the receipt of payments under the Royalty Purchase Agreement and the Medtronic Loan Agreement, and receipt of additional expected funds under the terms of the sale of Vivasure to Haemonetics. There are no assurances that any of these factors will be favorable to us, and we may need to seek additional sources of liquidity to meet our funding requirements earlier than current estimates, including the issuance of new equity, and/or other financing structures. In this regard, as of the date of this Annual Report on Form 10-K, we may sell up to $92.4 million of shares of our common stock under the sales agreement we entered into with TD Securities (USA) LLC (the "Sales Agreement").

Our future viability is dependent on our ability to raise additional capital to finance our operations. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurance that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all.

As noted above, the sale of our common stock pursuant to the Resale Registration Statement may result in a decline in the value of our common stock, which may make it more difficult and more dilutive to the existing holders of our common stock to raise funds from the sale of our equity securities.

Cash Flows

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

	Year Ended December 31,	
	2025	2024
Net cash used in operating activities	$ (48,963)	$ (50,558)
Net cash (used in) provided by investing activities	(26,941)	13,089
Net cash provided by financing activities	88,333	29,171
Net increase (decrease) in cash and cash equivalents	**$ 12,429**	**$ (8,298)**

Comparison of the Years Ended December 31, 2025 and 2024

Net Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2025 was $49.0 million and primarily consisted of our net loss of $52.7 million, partially offset by non-cash charges of $14.1 million and changes in net operating assets and liabilities of $10.4 million. Our non-cash charges primarily consisted of stock-based compensation of $12.0 million and $2.0 million in non-cash interest expense in liability related to the Royalty Purchase Agreement. The net change in operating assets and liabilities was primarily due to a decrease in deferred revenue of $15.4 million, partially offset by an increase in accounts payable, accrued expenses, and other liabilities of $4.9 million.

Net cash used in operating activities for the year ended December 31, 2024 was $50.6 million and primarily consisted of our net loss of $61.0 million, partially offset by non-cash charges of $11.2 million and changes in net operating assets and liabilities of $765,000. Our non-cash charges primarily consisted of stock-based compensation of $10.6 million and $1.0 million in acquired in-process research and development, partially offset by $1.5 million related to accretion and interest of marketable securities. The net change in operating assets and liabilities was primarily due to an increase in accounts payable, accrued expenses, and other liabilities of $3.0 million, partially offset by an increase in prepaid expenses and other assets of $1.1 million, a decrease in deferred revenue of $2.0 million, and a decrease in operating lease liabilities of $652,000.

Net Cash Flows from Investing Activities

Net cash (used in) provided by investing activities for the year ended December 31, 2025 was $26.9 million, which primarily consisted of the purchase of $76.3 million of marketable securities and $489,000 paid for purchases of property and equipment, partially offset by the sale of $49.9 million of marketable securities.

Net cash provided by investing activities for the year ended December 31, 2024 was $13.1 million, which primarily consisted of the sale of $86.6 million of marketable securities, partially offset by the purchase of $72.6 million of marketable securities, and $600,000 paid for an asset acquisition, net of cash acquired.

Net Cash Flows from Financing Activities

Net cash provided by financing activities of $88.3 million for the year ended December 31, 2025 primarily consisted of $57.8 million of proceeds from the sale of common stock and the pre-funded warrants, net of issuance costs and $20.0 million of proceeds from the sale of future royalties, $12.6 million of proceeds from the issuance of Series A Preferred Stock, partially offset by $1.6 million used to settle taxes associated with the vesting of restricted stock units.

Net cash provided by financing activities of $29.2 million for the year ended December 31, 2024 was primarily attributable to the proceeds of $15.0 million, net of issuance costs, from the at-the-market offering under the Open Market Sale Agreement℠ with Jefferies LLC and proceeds from the 2024 LSA with Hercules of $15.0 million. For additional information, see Note 16 to the Consolidated Financial Statements – *"Debt Financing."*

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments as of December 31, 2025 (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating lease obligations	$ 1,868	$ 881	$ 987	$ —	$ —
Debt, principal and interest[1]	19,229	1,445	17,784	—	—
Total	**$ 21,097**	**$ 2,326**	**$ 18,771**	**$ —**	**$ —**

(1) In November 2024, we entered into the 2024 LSA with Hercules, as amended. The 2024 LSA will mature in November 2028. Refer to Note 16 to the Consolidated Financial Statements for additional information.

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

Critical Accounting Policies and Estimates

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

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

Revenue Recognition

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

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

Partnership Revenues

To date, our partnership revenues have related to the Terumo Agreement described below. Pursuant to the terms of the Termination and ROFR Agreement, the Terumo Agreement was terminated on October 24, 2025. In future periods, partnership revenues may also include revenues related to the Medtronic Agreement, discussed in Note 4 to the Consolidated Financial Statements.

Orchestra BioMed, Inc. entered into the Terumo Agreement as further described in Note 3 to the Consolidated Financial Statements. We assessed whether the Terumo Agreement fell within the scope of ASC 808 based on whether the arrangement involved joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. We determined that the Terumo Agreement did not fall within the scope of ASC 808. We then analyzed the arrangement pursuant to the provisions of ASC 606 and determined that the arrangement represents a contract with a customer and is therefore within the scope of ASC 606.

The promised goods or services in the Terumo Agreement included (i) license rights to our intellectual property and (ii) research and development services. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources or (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct in the Terumo Agreement, we considered factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

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

The Terumo Agreement had contained development and regulatory milestone payments. At contract inception and at each reporting period, we evaluated whether the milestones were considered probable of being reached and estimated the amount to be included in the transaction price using the most likely amount method. If it was probable that a significant revenue reversal would not occur, the associated milestone value was included in the transaction price. At the end of each subsequent reporting period, we re-evaluated the probability of achievement of such development milestones and any related constraint, and if necessary, adjusted our estimate of the overall transaction price. Any such adjustments were recorded on a cumulative catch-up basis, which affected partnership revenues and earnings in the period of adjustment.

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

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

On October 28, 2025, we entered into the Termination and ROFR Agreement with Terumo with respect to Virtue SAB. The Termination and ROFR Agreement, which supersedes and terminates the Terumo Agreement, grants Terumo a ROFR to acquire the rights, or enter a distribution arrangement, with respect to Virtue SAB for the treatment of coronary artery disease, in exchange for an upfront payment of $10.0 million. In connection with the Termination and ROFR Agreement, Terumo invested an additional $20.0 million in Orchestra BioMed through our Series A Preferred Stock, which is convertible into common stock in the future, subject to certain conditions, at a minimum of $12 per share. Pursuant to the terms of the Termination and ROFR Agreement, we have no further performance obligations under the Terumo Agreement and therefore recognized the remaining amounts of deferred revenue. We recognized $30.0 million in cumulative partnership revenues from 2019 through December 31, 2025. In addition to recognizing the remainder of the deferred revenue, partnership revenue for the year ended December 31, 2025 included $10.0 million in consideration for the ROFR and $7.4 million associated with the premium above the fair market value of the Series A Preferred Stock.

In June 2022, Orchestra BioMed Inc., BackBeat Medical, LLC and Medtronic entered into the Medtronic Agreement for the development and commercialization of AVIM Therapy for the treatment of pacemaker-indicated patients with uncontrolled HTN despite the use of anti-hypertensive medications. We determined that the arrangement is a collaboration within the scope of ASC 808. In addition, we concluded Medtronic is a customer for a good or service that is a distinct unit of account, and therefore the transactions in the Medtronic Agreement should be accounted for under ASC 606. Through December 31, 2025, there have been no amounts recognized as revenue under the Medtronic Agreement.

Product Revenues

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

Research and Development Prepayments, Accruals and Related Expenses

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

Royalty purchase agreement

On July 31, 2025, we entered into the Royalty Purchase Agreement with Ligand. Under the terms of the Royalty Purchase Agreement, in exchange for the Investment Amount, less certain reimbursable expenses, Ligand acquired from us the right to receive Royalty Interest with respect to revenue (including certain licensing revenue) received by us in a calendar year in connection with Annual Net Sales of our Products in the field of coronary artery treatment.

Pursuant to the Royalty Purchase Agreement, the Investment Amount shall be paid in two tranches: (i) $20.0 million was paid on August 4, 2025 (the "Ligand Closing") and (ii) $15.0 million is payable on May 1, 2026 (the "Second Installment"), provided certain conditions have been met. In repayment of the Investment Amount, we will remit 17.0% of revenues related to the Products until an annual total of $17.0 million has been remitted to Ligand, thereafter we will remit (a) 4.0% of revenues related to the Primary Product in the field of hypertension treatment and (b) 4.0% of revenues related to the Secondary Product in the field of coronary artery treatment. In addition, under the terms of the Royalty Purchase Agreement, unless and until Ligand pays the Second Installment, Ligand shall only be entitled to 57.1% of the amounts it would otherwise be due under the Royalty Purchase Agreement. However, regardless of whether the Second Installment has been paid, under the terms of the Royalty Purchase Agreement, the percentages referenced in the second sentence of this paragraph will incrementally increase from 17.0% and 4.0% up to 20.0% and 7.0%, respectively, if we do not achieve certain enrollment milestones relating to the BACKBEAT clinical study through January 1, 2027.

We accounted for the sale of royalty revenues to Ligand, pursuant to the Royalty Purchase Agreement, in accordance with ASC 470, *Debt*, which addresses situations in which an entity receives cash from an investor in return for an agreement to pay the investor a specified percentage of the revenue from a contractual right. We classified the proceeds received from the sale to Ligand as debt as we determined that it had significant continuing involvement in the generation of the cash flows to Ligand. Interest related to the Royalty Purchase Agreement is recognized utilizing the effective interest method over the estimated term. When the Second Installment is received, it will also be recorded as a liability related to the sale of future royalties when they are received and amortized under the effective interest method over the estimated remaining term of the Royalty Purchase Agreement.

As of the Ligand Closing, our estimate of this total interest expense associated with the Royalty Interest resulted in an effective annual interest rate of approximately 23.1%. This estimate contains significant assumptions that impact both the amount recorded at execution and the interest expense that will be recognized over the royalty period. We will periodically assess the estimated amounts due and payable to Ligand and to the extent that the amount or timing of such payments is materially different than the original estimates, an adjustment will be recorded prospectively to the consolidated statements of operations and comprehensive loss. There are a number of factors that could materially affect the amount and timing of the royalty payments to be paid by us to Ligand and, correspondingly, the amount of interest expense recorded by us.

Series A Preferred Stock

On November 7, 2025, we entered into a preferred stock purchase agreement, pursuant to which we agreed to issue 200,000 shares of our Series A Preferred Stock at a price per share equal to $100.00 for an aggregate amount of $20.0 million. The Series A Preferred Stock contains certain conversion and redemption features. We utilized an option pricing valuation to determine the fair value of the Series A Preferred Stock at issuance. The valuation incorporated Level 3 inputs in the fair value hierarchy including the expected life of Series A Preferred Stock, expected volatility, and discount rate as well as probability-weighted outcomes. Assumptions used in the valuation also take into account the contractual terms as well as the quoted price of our common stock in an active market. Significant changes in any of these inputs in isolation would result in significant changes to the fair value measurement.

Derivative Liability

In connection with the issuance of the Series A Preferred Stock, we evaluated the instruments for any features that must be bifurcated and separately accounted for as embedded derivatives. We concluded that certain conversion and redemption features meet the requirements to be separately accounted for as a bifurcated derivative. The Series A Preferred Stock was accounted for as mezzanine equity in accordance with ASC 480, *Distinguishing Liabilities from Equity ("ASC 480")* and the embedded conversion and redemption features were separated from the host instrument and recognized as a derivative liability with the change in fair value at each reporting period end recognized in the consolidated statements of operations and comprehensive loss.

We performed a "with-and-without" scenario analysis to determine the fair value of the derivative liability by comparing the value of the Series A Preferred Stock including the bifurcated embedded derivatives to the value of the Series A Preferred Stock excluding them. We utilized an option pricing valuation with the expected life of Series A Preferred Stock, expected volatility, and discount rate as significant inputs as well as probability-weighted outcomes. Assumptions used in the valuation also take into account the contractual terms as well as the quoted price of our common stock in an active market. Significant changes in any of those inputs in isolation would result in significant changes to the fair value measurement.

Stock-Based Compensation

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

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

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

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

- *Expected Volatility* — We consummated the Business Combination on January 26, 2023 and lack sufficient company-specific historical and implied volatility information. Therefore, we derived expected stock volatility using a weighted average blend of historical volatility of comparable peer public companies and our own historical volatility, over a period equivalent to the expected term of the stock-based awards.

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

- *Expected Dividend Yield* — The expected dividend yield is zero as we have not paid, and we do not anticipate paying any dividends on our common stock in the foreseeable future.

- *Common Stock Valuation* — We determine the fair value of our common stock based on the closing price of our common stock on the date of grant.

During the years ended December 31, 2025 and 2024, stock-based compensation was $12.0 million and $10.6 million, respectively. As of December 31, 2025, we had approximately $13.3 million of total unrecognized stock-based compensation, which we expect to recognize over a weighted-average period of approximately 2.3 years.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2, *"Summary of Significant Accounting Policies,"* to the Consolidated Financial Statements.

Smaller Reporting Company Status

We are a "smaller reporting company" as defined in the Exchange Act. As a smaller reporting company, we will continue to not be required to comply with the auditor attestation requirements of Section 404(a) of the Sarbanes-Oxley Act of 2002 as long as (a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting common stock held by non-affiliates is less than $700.0 million as of the last business day of the second quarter of such fiscal year. We may also take advantage of certain reduced disclosure requirements as a smaller reporting company, including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We will be able to take advantage of these scaled disclosures for so long as (i) the market value of our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or (ii)(a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting common stock held by non-affiliates is less than $700.0 million as of the last business day of the second quarter of such fiscal year.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

As a smaller reporting company, we are not required to provide the information requested by this Item.

Item 8. Financial Statements and Supplementary Data

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Orchestra BioMed Holdings, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Orchestra BioMed Holdings, Inc. (the Company) as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2025, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2025, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Subsequent Measurement of Royalty Purchase Agreement Liability

Description of the Matter

As described in Note 15 of the consolidated financial statements, the Company entered into a revenue participation right purchase and sale agreement (the "Royalty Purchase Agreement") with Ligand. The Company accounted for its sale of revenue participation rights as debt, initially recorded at the proceeds received. Subsequently, the liability is measured using the effective interest method over the expected term of the arrangement. Each reporting period, management estimates the amount and timing of future revenues that need to be paid to Ligand and applies the interest method to determine the measurement of the liability and interest expense to be recognized. The carrying amount of the Royalty Purchase Agreement liability was $16.5 million as of December 31, 2025 and the interest expense recorded was $2.0 million for the period ended December 31, 2025.

Auditing the subsequent measurement of the Royalty Purchase Agreement liability and related interest expense was complex and involved a high degree of subjectivity, as the recorded amounts were dependent on management's estimates of the timing and amount of future royalty payments. These estimates were based on significant assumptions related to the probability of success of the related product candidates and the future projected revenues, which involved significant judgment and estimation uncertainty.

How We Addressed the Matter in Our Audit

To test the subsequent measurement of the Royalty Purchase Agreement liability and related interest expense, our audit procedures included, among others, evaluating the significant assumptions discussed above and testing the completeness and accuracy of the underlying data used by management in its analysis. For example, we corroborated certain of management's assumptions to publicly available information and third-party market research studies. In addition, we performed sensitivity analyses over the significant assumptions to evaluate the changes in the measurement of the Royalty Purchase Agreement liability and related interest expense that would result from changes in the significant assumptions.

Valuation of Series A Preferred Stock and Embedded Derivative Liability

Description of the Matter

As described in Notes 3, 8 and 9 of the consolidated financial statements, the Company issued Series A Preferred Stock in November 2025 to Terumo. Series A Preferred Stock provides Terumo options to redeem the preferred stock for cash or convert it into common stock upon occurrence of certain events or conditions. The Company classified Series A Preferred Stock as mezzanine equity and recorded the preferred stock initially at its fair value of $12.6 million. In addition, the options required bifurcation as a derivative liability measured at fair value each reporting period, with changes in the fair value reported in earnings. The Company utilized an option pricing model to determine the fair value of the Series A Preferred Stock at issuance, which required the use of significant unobservable inputs such as the expected life of Series A Preferred Stock, expected volatility, discount rate and probability-weighted outcomes. At each reporting date, management performs a "with-and-without" scenario analysis to determine the fair value of the derivative liability by comparing the value of the preferred stock including the bifurcated embedded derivatives to the value of the preferred stock excluding them. The embedded derivative liability is classified as level 3 in the fair value hierarchy because it is valued using significant unobservable inputs mentioned above. At December 31, 2025, the fair value of the embedded derivative liability was $2.7 million.

Auditing the valuation of the Series A Preferred Stock and the bifurcated derivative liability was challenging as the Company uses complex valuation methodologies that use significant unobservable inputs discussed above and includes significant assumptions about economic and market conditions with uncertain future outcomes.

How We Addressed the Matter in Our Audit

To test the estimated fair value of the Series A Preferred Stock at issuance as well as the fair value of the bifurcated derivative liability on each reporting date, we performed audit procedures that included, among other procedures, assessing the valuation methodologies and the significant inputs and assumptions discussed above, and testing the completeness and accuracy of the underlying data used by management in its estimates. For example, we compared the significant assumptions used by management to current market information and performed sensitivity analyses of significant inputs and assumptions to evaluate the changes in the fair value of the Series A Preferred Stock and the bifurcated derivative liability that would result from changes in the inputs and assumptions. We also involved internal valuation specialists to assist in our evaluation of the significant inputs and assumptions and methodologies used by management and to develop an independent valuation of the preferred stock and the bifurcated derivative liability.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.

Philadelphia, Pennsylvania

March 12, 2026

ORCHESTRA BIOMED HOLDINGS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2025	December 31, 2024
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 34,690	$ 22,261
Marketable securities	71,822	44,551
Accounts receivable, net	95	92
Inventory	310	173
Prepaid expenses and other current assets	994	2,094
Total current assets	107,911	69,171
Property and equipment, net	1,715	1,384
Right-of-use assets	1,496	2,103
Strategic investments	2,495	2,495
Deposits and other assets	1,240	1,020
TOTAL ASSETS	$ 114,857	$ 76,173
LIABILITIES, SERIES A PREFERRED STOCK AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 6,095	$ 5,134
Accrued expenses and other liabilities	9,890	6,084
Operating lease liability, current portion	751	550
Deferred revenue, current portion	—	4,439
Total current liabilities	16,736	16,207
Deferred revenue, less current portion	—	10,989
Royalty purchase agreement	16,482	—
Loan payable	14,268	14,292
Derivative liability	2,749	—
Operating lease liability, less current portion	936	1,687
Other long-term liabilities	308	40
TOTAL LIABILITIES	51,479	43,215
Series A Preferred Stock, $0.0001 par value per share; 200,000 issued and outstanding at December 31, 2025 and 0 issued and outstanding at December 31, 2024; aggregate liquidation preference of $20,000 at December 31, 2025	9,808	—
STOCKHOLDERS' EQUITY		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized;	—	—
Common stock, $0.0001 par value per share; 340,000,000 shares authorized; 57,032,963 and 38,194,442 shares issued and outstanding as of December 31, 2025 and December 31, 2024, respectively.	6	4
Additional paid-in capital	416,083	342,780
Accumulated other comprehensive income	60	52
Accumulated deficit	(362,579)	(309,878)
TOTAL STOCKHOLDERS' EQUITY	53,570	32,958
TOTAL LIABILITIES, SERIES A PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 114,857	$ 76,173

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2025	**2024**
Revenue:		
Partnership revenue	$ 32,871	$ 2,005
Product revenue	611	633
Total revenue	33,482	2,638
Expenses:		
Cost of product revenues	190	204
Research and development	58,185	42,804
Selling, general and administrative	26,914	23,931
Total expenses	85,289	66,939
Loss from operations	(51,807)	(64,301)
Other (expense) income:		
Interest (expense) income, net	(1,148)	3,356
Change in the fair value of derivative liability	254	—
Loss on fair value of strategic investments	—	(68)
Other expense	—	(11)
Total other (expense) income	(894)	3,277
Net loss	(52,701)	(61,024)
Adjustment to carrying value of Series A Preferred Stock	(254)	—
Net loss attributable to common stockholders	$ (52,955)	$ (61,024)
Net loss attributable to common stockholders per share		
Basic and diluted	$ (1.11)	$ (1.66)
Weighted-average shares used in computing net loss attributable to common stockholders per share, basic and diluted	47,747,078	36,821,042
Comprehensive loss		
Net loss	$ (52,701)	$ (61,024)
Unrealized gain on marketable securities	8	62
Comprehensive loss	$ (52,693)	$ (60,962)

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.
Consolidated Statements of Stockholders' Equity
(in thousands, except share and per share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance, January 1, 2024	35,777,412	$ 4	$ 316,903	$ (10)	$ (248,854)	$ 68,043
At-the-Market offering, net of offering costs $465	2,000,000	—	15,035	—	—	15,035
Shares issued pursuant to an asset acquisition	70,621	—	352	—	—	352
Unrealized gain on marketable securities	—	—	—	62	—	62
Stock-based compensation	—	—	10,615	—	—	10,615
Restricted stock unit vesting	289,550	—	(550)	—	—	(550)
Exercise of stock options	56,859	—	240	—	—	240
Issuance of warrants pursuant to debt financing	—	—	185	—	—	185
Net loss	—	—	—	—	(61,024)	(61,024)
Balance, December 31, 2024	38,194,442	$ 4	$ 342,780	$ 52	$ (309,878)	$ 32,958
Issuance of common stock and pre-funded warrants in private placement, net of issuance costs of $4,635	17,624,027	2	57,778	—	—	57,780
At-the-Market offering, net of issuance costs of $43	382,024	—	1,543	—	—	1,543
Unrealized gain on marketable securities	—	—	—	8	—	8
Stock-based compensation	—	—	11,978	—	—	11,978
Restricted stock unit vesting	810,358	—	(1,552)	—	—	(1,552)
Exercise of stock options	22,112	—	91	—	—	91
Issuance of warrants pursuant to debt financing	—	—	239	—	—	239
Issuance of warrants pursuant to royalty purchase agreement	—	—	3,480	—	—	3,480
Adjustment to carrying value of Series A Preferred Stock	—	—	(254)	—	—	(254)
Net loss	—	—	—	—	(52,701)	(52,701)
Balance, December 31, 2025	57,032,963	$ 6	$ 416,083	$ 60	$ (362,579)	$ 53,570

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.
Consolidated Statements of Cash Flows
(in thousands, except share and per share data)

	Year Ended December 31,	
	2025	**2024**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (52,701)	$ (61,024)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	327	308
Stock-based compensation	11,978	10,615
Acquired in-process research and development	—	1,045
Loss on fair value of strategic investments	—	68
Non-cash interest expense on liability related to the royalty purchase agreement	2,048	—
Accretion and interest related to marketable securities	(811)	(1,501)
Non-cash lease expense	607	654
Change in the fair value of derivative liability	(254)	—
Amortization of deferred financing fees	215	31
Other	—	11
Changes in operating assets and liabilities:		
Accounts receivable	(3)	22
Inventory	(137)	(28)
Prepaid expenses and other assets	880	(1,071)
Accounts payable, accrued expenses and other liabilities	4,866	2,969
Operating lease liabilities – current and non-current	(550)	(652)
Deferred revenue	(15,428)	(2,005)
Net cash used in operating activities	(48,963)	(50,558)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(489)	(289)
Sales of marketable securities	49,860	86,628
Purchases of marketable securities	(76,312)	(72,648)
Asset acquisition, net of cash acquired	—	(602)
Net cash (used in) provided by investing activities	(26,941)	13,089
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from sale of common stock and pre-funded warrants, net of issuance costs	57,780	—
Proceeds from the royalty purchase agreement	20,000	—
Proceeds from issuance of Series A preferred stock	12,557	—
Repayment of royalty liability	(972)	—
Proceeds from Hercules term loan	—	15,000
Proceeds from At-The-Market offering, net of issuance costs	1,543	15,035
Proceeds from exercise of stock options	91	240
Restricted stock units withheld for tax	(1,552)	(550)
Deferred financing costs	(1,114)	(554)
Net cash provided by financing activities	88,333	29,171
Net increase (decrease) in cash and cash equivalents	12,429	(8,298)
Cash and cash equivalents, beginning of the period	22,261	30,559
Cash and cash equivalents, end of the period	$ 34,690	$ 22,261
Supplemental Disclosures of Cash Flow Information		
Cash paid during the year ended December 31:		
Interest	$ 1,447	$ 102
Supplemental disclosure of noncash activities		
Operating lease right-of-use asset obtained in exchange for new operating lease liabilities	$ —	$ 1,202
Increase in accounts payable, accrued expenses and other liabilities related to fixed assets	$ 169	$ —
Common stock issued pursuant to asset acquisition	$ —	$ 352
Warrants issued pursuant to debt financing	$ 239	$ 185
Warrants issued pursuant to the royalty purchase agreement	$ 3,480	$ —

The accompanying notes are an integral part of these consolidated financial statements.

ORCHESTRA BIOMED HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Orchestra BioMed Holdings, Inc. (collectively, with its subsidiaries, "Orchestra" or the "Company") is a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. The Company's partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products it develops. The Company's flagship product candidates are Atrioventricular Interval Modulation Therapy ("AVIM Therapy") for the treatment of hypertension ("HTN"), the leading risk factor for death worldwide, and Virtue® Sirolimus AngioInfusion™ Balloon ("Virtue SAB") for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide.

The Company was incorporated in the Cayman Islands in 2020, as a special purpose acquisition company under the name Health Sciences Acquisitions Corporation 2 ("HSAC2"). On January 26, 2023, Orchestra BioMed, Inc., the Company's wholly owned subsidiary, and HSAC2 consummated a business combination pursuant to which, among other things, Orchestra BioMed, Inc. became a wholly owned subsidiary of HSAC2 and HSAC2 changed its name to Orchestra BioMed Holdings, Inc. (the "Business Combination"). HSAC2 Holdings, LLC (the "Sponsor") was the sponsor of HSAC2 prior to the Business Combination.

Orchestra BioMed, Inc. was incorporated in Delaware in January 2017 and was formed to acquire operating and other assets as well as to raise capital conducted through private placements. In May 2018, Orchestra BioMed, Inc. concurrently completed its formation mergers (the "Formation Mergers") with Caliber Therapeutics, Inc., a Delaware corporation, BackBeat Medical, Inc., a Delaware Corporation, and FreeHold Surgical, Inc., a Delaware corporation. Orchestra BioMed, Inc. completed the conversions of BackBeat Medical, Inc. to BackBeat Medical, LLC ("BackBeat"), a Delaware limited liability company, of FreeHold Surgical, Inc. to FreeHold Surgical, LLC ("FreeHold") and of Caliber Therapeutics, Inc. to Caliber Therapeutics, LLC ("Caliber"), a Delaware limited liability company, in 2019.

Caliber

Caliber Therapeutics, Inc. was incorporated in Delaware in October 2005 and began development of its lead product Virtue SAB in 2008. Virtue SAB is a patented drug/device combination product candidate for the treatment of artery disease that delivers a proprietary extended release formulation of sirolimus called SirolimusEFR to the vessel wall during balloon angioplasty without any coating on the balloon surface or the need for leaving a permanent implant such as a stent in the artery.

BackBeat

BackBeat Medical, Inc. was incorporated in Delaware in January 2010 and began development of its lead product AVIM Therapy that same year. AVIM Therapy is a patented implantable cardiac stimulation-based treatment for HTN that is designed to immediately, substantially and persistently lower blood pressure while simultaneously modulating autonomic nervous system responses that normally drive and maintain blood pressure higher. Refer to Note 4 for details regarding the Exclusive License and Collaboration Agreement, dated as of June 30, 2022, by and among, Orchestra BioMed, Inc., BackBeat and Medtronic, Inc. (an affiliate of Medtronic plc) (the "Medtronic Agreement").

FreeHold

FreeHold Surgical, Inc. was incorporated in Delaware in May 2010 and began development of its hands-free, intracorporeal retractor device for minimally-invasive surgery in 2012. FreeHold is engaged in the development, sales and marketing of its retractor products that provide optimized visual and total surgeon control during laparoscopic and robotic procedures.

Basis of Presentation and Liquidity

The accompanying consolidated financial statements herein have been prepared by the Company in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

The Company has a limited operating history and the sales and income potential of its businesses and markets are unproven. As of December 31, 2025, the Company had an accumulated deficit of $362.6 million and has experienced net losses each year since its inception. The Company expects to incur substantial operating losses in future periods and will require additional capital as it seeks to advance its products to commercialization. The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biomedical device industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding, and history of operating losses.

The Company follows the provisions of Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 205-40, *Presentation of Financial Statements — Going Concern*, which requires management to assess the Company's ability to continue as a going concern within one year after the date the financial statements are issued.

Based on the available balance of cash and cash equivalents and marketable securities as of December 31, 2025, subsequent proceeds received (see Note 19 – *"Subsequent Events"*), and expected future proceeds from contractual financing commitments, management has concluded that sufficient capital is available to fund its operations and meet cash requirements through the one-year period subsequent to the issuance date of these financial statements. Management may consider plans to raise capital through the one-year period subsequent to the issuance date of these financial statements through issuance of equity securities, debt securities, and/or additional development and commercialization partnerships for other products within the Company's development pipeline. The source, timing and availability of any future financing will depend principally upon market conditions and on the progress of the Company's research and development programs.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates. Areas where significant estimates exist include, but are not limited to, the fair value of stock-based compensation, research and development costs incurred, effective interest expense related to the Royalty Purchase Agreement (see Note 15 – *"Royalty Purchase Agreement"* for additional information), the fair value of Series A Preferred Stock (see Note 8 – *"Common and Preferred Stock"* for additional information), and the fair value of the derivative liability related to the Series A Preferred Stock (see Note 9 – *"Derivative Liability"* for additional information).

Cash and Cash Equivalents

Cash and cash equivalents are held in banks or in custodial accounts with banks. Cash equivalents are defined as all liquid investments and money market funds with maturity from date of purchase of 90 days or less that are readily convertible into cash.

Marketable Securities

The Company accounts for its marketable securities with remaining maturities of less than one year, or where its intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. These investments represent debt investments in corporate or government securities that are designated as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders' equity as accumulated other comprehensive income (loss). The disclosed fair value related to the Company's investments is based on market prices from a variety of industry standard data providers and generally represent quoted prices for similar assets in active markets or have been derived from observable market data.

Strategic Investments

Management has made investments in certain companies and assesses whether the Company exerts significant influence over its strategic investments. The Company considers the nature and magnitude of its investment, any voting and protective rights it holds, any participation in the governance of the other company, and other relevant factors such as the presence of a collaboration or other business relationships. To date, the Company has concluded that it does not have the ability to exercise significant influence over its strategic investments.

The Company's strategic investments consist of preferred shares of Vivasure Medical Limited ("Vivasure"), a privately-held company and related party. The investments in Vivasure do not have readily determinable fair values and are recorded at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for identical or similar investments of the same issuer. Additionally, as the investments in Vivasure are not readily marketable, the Company categorized the investments as non-current assets. As of December 31, 2025 and 2024, the carrying value of the investments in Vivasure was $2.5 million. For an update to this investment, see Note 19 – *"Subsequent Events."*

Fair Value of Financial Instruments

The Company applies ASC 820, *Fair Value Measurement* ("ASC 820"), which establishes a framework for measuring fair value and clarifies the definition of fair value within that framework. ASC 820 defines fair value as an exit price, which is the price that would be received for an asset or paid to transfer a liability in the Company's principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value hierarchy established in ASC 820 generally requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Observable inputs reflect the assumptions that market participants would use in pricing the asset or liability and are developed based on market data obtained from sources independent of the reporting entity. Unobservable inputs reflect the entity's own assumptions based on market data and the entity's judgments about the assumptions that market participants would use in pricing the asset or liability and are to be developed based on the best information available in the circumstances.

The carrying value of the Company's cash and cash equivalents, accounts receivable, prepaid expense, accounts payable and accrued expenses approximate fair value because of the short-term maturity of these financial instruments. In addition, the Company records its investment in marketable securities at fair value. See Note 5 – *"Financial Instruments and Fair Value Measurements"* for additional information regarding fair value measurements. For additional information on the fair value measurements performed as part of the Series A Preferred Stock issuance, see Note 8 – *"Common and Preferred Stock."*

The valuation hierarchy is composed of three levels. The classification within the valuation hierarchy is based on the lowest level of input that is significant to the fair value measurement. The levels within the valuation hierarchy are described below:

Level 1 — Assets and liabilities with unadjusted, quoted prices listed on active market exchanges. Inputs to the fair value measurement are observable inputs, such as quoted prices in active markets for identical assets or liabilities.

Level 2 — Inputs to the fair value measurement are determined using prices for recently traded assets and liabilities with similar underlying terms, as well as direct or indirect observable inputs, such as interest rates and yield curves that are observable at commonly quoted intervals.

Level 3 — Inputs to the fair value measurement are unobservable inputs, such as estimates, assumptions, and valuation techniques when little or no market data exists for the assets or liabilities.

Accounts Receivable and Allowance for Doubtful Accounts

Accounts receivable represent amounts due from customers. The allowance for doubtful accounts is recorded for estimated losses by evaluating various factors, including relative creditworthiness of each customer, historical collections experience and aging of the receivable. As of December 31, 2025 and 2024, an allowance for doubtful accounts was not deemed necessary.

Inventory

Inventory is stated at the lower of standard cost (which approximates actual cost on a first-in, first-out basis) and net realizable value. Net realizable value represents the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal and transportation. The Company analyzes its inventory levels and writes down inventory that has become obsolete or has a cost basis in excess of its expected net realizable value or inventory quantities in excess of expected requirements. Excess requirements are determined based on comparison of existing inventories to forecasted sales, with consideration given to inventory shelf life. Expired inventory is disposed of, and the related costs are recognized in cost of goods sold. As of December 31, 2025 and 2024, an impairment charge as a result of obsolete inventory was not deemed necessary.

Research and Development Prepayments, Accruals and Related Expenses

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

Asset Acquisitions and Acquired In-Process Research and Development Expenses

The Company accounts for acquisitions of assets or a group of assets that do not meet the definition of a business as asset acquisitions. Asset acquisitions are based on the cost to acquire the asset or group of assets, which include certain transaction costs. In an asset acquisition, the cost to acquire is allocated to the identifiable assets acquired and liabilities assumed based on their relative fair values as of the acquisition date. No goodwill is recorded in an asset acquisition. Assets that are acquired in an asset acquisition for use in research and development activities that have an alternative future use are capitalized as in-process research and development ("IPR&D"). Acquired IPR&D that has no alternative future use as of the acquisition date is recognized as research and development expense as of the acquisition date. The Company recognized $1.0 million of IPR&D expense for the year ended December 31, 2024. No IPR&D expense was recognized during the year ended December 31, 2025.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets. Leasehold improvements are amortized over the lesser of their useful life or the remaining life of the lease. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Maintenance and repairs are charged to operations as incurred.

Asset category	Depreciable life
Manufacturing equipment	10 years
Office equipment	3 – 7 years
Research and development equipment	7 years

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the terms of the arrangement. The Company accounts for a contract as a lease when it has the right to control the asset for a period of time while obtaining substantially all of the asset's economic benefits. The Company determines the initial classification and measurement of its operating right-of-use ("ROU") assets and operating lease liabilities at the lease commencement date, and thereafter if modified. The lease term includes any renewal options that the Company is reasonably assured to exercise. The Company's policy is to not record leases with a lease term of 12 months or less on its balance sheets.

The ROU asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, the Company uses its estimated secured incremental borrowing rate for that lease term. Lease expense for operating leases is recognized on a straight-line basis over the reasonably assured lease term based on the total lease payments and is included in operating expense in the consolidated statements of operations and comprehensive loss.

Payments due under each lease agreement include fixed and variable payments. Variable payments relate to the Company's share of the lessor's operating costs associated with the underlying asset and are recognized when the event on which those payments are assessed occurs. Variable payments have been excluded from the lease liability and associated right-of-use asset.

The interest rate implicit in lease agreements is typically not readily determinable, and as such, the Company utilizes the incremental borrowing rate to calculate lease liabilities, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

Debt Discount and Debt Issuance Costs

Debt discounts and debt issuance costs incurred in connection with the issuance of debt are capitalized and reflected as a reduction to the related debt liability. The costs are amortized to interest expense over the term of the debt using the effective-interest method.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. The Company has not identified any such impairment losses to date.

Revenue Recognition

The Company recognizes revenue under the core principle according to ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), to depict the transfer of control to the Company's customers in an amount reflecting the consideration the Company expects to be entitled to. In order to achieve that core principle, the Company applies the following five step approach: (1) identify the contract with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when a performance obligation is satisfied.

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

Partnership Revenues

To date, the Company's partnership revenues have related to the Terumo Agreement as further described in Note 3.

The Company assessed whether the Terumo Agreement fell within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808") based on whether the arrangement involved joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. The Company determined that the Terumo Agreement did not fall within the scope of ASC 808. The Company then analyzed the arrangement pursuant to the provisions of ASC 606 and determined that the arrangement represents a contract with a customer and is therefore within the scope of ASC 606.

The promised goods or services in the Terumo Agreement had included (i) license rights to the Company's intellectual property, and (ii) research and development services. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources or (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services were distinct in the Terumo Agreement, the Company considered factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

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

The Company has determined that intellectual property that was licensed to Terumo and the research and development services provided to support the premarket approval by the U.S. Food and Drug Administration (the "FDA") for the in-stent restenosis ("ISR") indication represented a combined performance obligation that was satisfied over time, and that the appropriate method of measuring progress for purposes of recognizing revenues related to a proportional performance model that measured the proportional performance based on the costs incurred to date relative to the total costs expected to be incurred through the completion of the performance obligation. The Company evaluated the measure of progress at each reporting period and, if necessary, adjusted the measure of performance and related revenue recognition.

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

On October 24, 2025, the Terumo Agreement was terminated pursuant to a termination and right of first refusal agreement (the "Termination and ROFR Agreement"). In future periods, partnership revenues may also include revenues related to the Medtronic Agreement as discussed in Note 4.

Product Revenues

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

Stock-Based Compensation

The Company applies ASC 718-10, *Compensation — Stock Compensation*, which requires the measurement and recognition of compensation expenses for all stock-based payment awards made to employees and directors including employee stock options under the Company's stock plans based on estimated fair values (see Note 11 – *"Stock-Based Compensation"*). Each award vests over the subsequent period during which the recipient is required to provide service in exchange for the award (the vesting period). The cost of each award is recognized as an expense in the financial statements over the respective vesting period on a straight-line basis.

Under the requirements of ASU 2018-07, the Company accounts for stock-based compensation to nonemployees under the fair value method, which requires all such compensation to be calculated based on the fair value at the measurement date (generally the grant date) and recognized in the Company's consolidated statements of operations and comprehensive loss over the requisite service period. The Company accounts for forfeitures of stock-based awards as they occur.

Series A Preferred Stock

The Company applies ASC 480-10, *Distinguishing Liabilities from Equity ("ASC 480")* which requires an evaluation to determine if liability classification is required for redeemable convertible stock. Liability classification is required for freestanding financial instruments that are (1) subject to an unconditional obligation requiring the issuer to redeem the instrument by transferring assets, such as those that are mandatorily redeemable, (2) instruments other than equity shares that embody an obligation of the issuer to repurchase its equity shares, or (3) certain types of instruments that obligate the issuer to issue a variable number of equity shares.

Securities that do not meet the scoping criteria to be classified as a liability under ASC 480 are subject to redeemable equity guidance, which prescribes that securities that may be subject to redemption upon an event not solely within the Company's control should be classified as mezzanine equity. Securities classified in mezzanine equity are initially measured at the fair value, net of issuance costs and excluding the fair value of bifurcated embedded derivatives, if any. Subsequent measurement is required when the combined initial amount recorded in mezzanine equity and its related derivative liability is more than the period end carrying amount. Adjustments to the carrying amount are charged to retained earnings (or additional paid in capital if there are no retained earnings) and do not affect net loss or comprehensive loss in the consolidated financial statements. Subsequent measurement of the carrying value of the redeemable convertible preferred stock is also required when the instrument is probable of becoming redeemable. The Company will accrete the redeemable convertible preferred stock to its redemption value once the instrument is probable of becoming redeemable. In certain circumstances, the redemption price may vary based on changes in stock price, in which case the Company recognizes changes in the redemption value immediately as they occur and adjusts the carrying value of the security to equal the then current maximum redemption value at the end of each reporting period.

Derivative Liability

The Company evaluates all its financial instruments, including convertible debt and redeemable convertible preferred stock, to determine if such instruments are derivatives or contain features that qualify as embedded derivatives. The Company applies significant judgment to identify and evaluate complex terms and conditions in these contracts and agreements to determine whether embedded derivatives exist. Embedded derivatives must be separately measured from the host contracts if all the requirements for bifurcation are met. The assessment of the conditions surrounding the bifurcation of embedded derivatives depends on the nature of the host contract. Bifurcated embedded derivatives are recognized at fair value, with changes in fair value recognized in the consolidated statements of operations and comprehensive loss at each reporting period end. Bifurcated embedded derivatives are classified as a separate liability in the consolidated balance sheets.

The Company's derivative liability are related to the conversion features embedded in the Series A Preferred Stock. See Note 8 – *"Common and Preferred Stock"* for additional information.

Net Loss Per Share

Basic net loss per share is calculated by dividing net loss less the adjustment to carrying value of Series A Preferred Stock by the weighted-average number of shares of common stock outstanding for the period, without consideration of potential dilutive shares of common stock. Since the Company was in a loss position for the periods presented, basic net loss is the same as diluted net loss since the effects of potentially dilutive securities are antidilutive. Potentially dilutive securities include all outstanding warrants, stock options, Earnout Consideration (see Note 18 – *"Net Loss Per Share"*), unvested restricted stock awards, convertible preferred shares (see Note 8 – *"Common and Preferred Stock"*) and restricted stock units. Shares of Company Common Stock outstanding but subject to forfeiture and cancellation by the Company (e.g., the Forfeitable Shares (as defined in Note 18)) are excluded from the weighted-average number of shares until the period in which such shares are no longer subject to forfeiture. Pre-funded warrants (see Note 10 – *"Warrants"*) are considered outstanding for the purposes of computing basic and diluted net loss per share because shares may be issued for little or no additional consideration and are fully vested and exercisable after the original issuance date of the pre-funded warrant. In periods in which there is net income, the Company would apply the two-class method to compute net income per share. Under this method, earnings are allocated to common stock and participating securities based on their respective rights to receive dividends, as if all undistributed earnings for the period were distributed. The two-class method does not apply in periods in which a net loss is reported.

Income Taxes

The Company accounts for income taxes using the asset-and-liability method in accordance with ASC 740, *Income Taxes* ("ASC 740"). Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on the deferred tax assets and liabilities of a change in tax rate is recognized in the period that includes the enactment date. A valuation allowance is recorded if it is more-likely-than-not that some portion or all the deferred tax assets will not be realized in future periods. At December 31, 2025 and 2024, the Company recorded a full valuation allowance on its deferred tax assets.

The Company follows the guidance in ASC Topic 740-10 in assessing uncertain tax positions. The standard applies to all tax positions and clarifies the recognition of tax benefits in the financial statements by providing for a two-step approach of recognition and measurement. The first step involves assessing whether the tax position is more-likely-than-not to be sustained upon examination based upon its technical merits. The second step involves measurement of the amount to be recognized. Tax positions that meet the more-likely than-not threshold are measured at the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate finalization with the taxing authority. The Company recognizes the impact of an uncertain income tax position in the financial statements if it believes that the position is more likely than not to be sustained by the relevant taxing authority. The Company will recognize interest and penalties related to tax positions in income tax expense as applicable.

Defined Contribution Plan

The Company has a defined retirement savings plan under Section 401(k) of the Internal Revenue Code. This plan allows eligible employees to defer a portion of their annual compensation on a pre-tax basis. Effective January 1, 2023, the Company participates in a matching safe harbor 401(k) Plan with a Company contribution of up to 3.5% of each eligible participating employee's compensation. Safe harbor contributions vest immediately for each participant. During the years ended December 31, 2025 and 2024, the Company made $426,000 and $380,000, respectively, in contributions under this safe harbor 401(k) Plan.

Comprehensive Loss

Comprehensive loss is comprised of net loss and changes in unrealized gains and losses on the Company's available-for-sale investments.

Segment Reporting

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company has determined it operates in one segment. For further discussion on Segment Reporting, see Note 17 – *"Segment Disclosures."*

New Accounting Standards

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires additional income tax disclosures in the annual consolidated financial statements. The amendments in ASU 2023-09 are intended to enhance the transparency and decision usefulness of income tax disclosures. For public entities, ASU 2023-09 is effective for annual periods beginning after December 15, 2024, with early adoption permitted. ASU 2023-09 was adopted prospectively and is effective for all annual periods beginning after December 15, 2024. There was no material effect on the Company's consolidated financial statements and disclosures.

In November 2024, the FASB issued ASU 2024-03, *Disaggregation of Income Statement Expenses* ("ASU 2024-03") to improve the disclosures about a public business entity's expenses and address requests from investors for more detailed information about the types of expenses in commonly presented expense captions. ASU 2024-03 is effective for annual reporting periods beginning after December 15, 2026. Early adoption is permitted. The Company is currently evaluating the impact of adopting ASU 2024-03 on its consolidated financial statements

3. Terumo Agreement

In June 2019, Orchestra BioMed, Inc. entered into a distribution agreement with Terumo Corporation ("Terumo Corporation") and Terumo Medical Corporation ("TMC" and, collectively with Terumo Corporation, "Terumo") for global development and commercialization of Virtue SAB in coronary and peripheral vascular indications (the "Terumo Agreement"). Under the Terumo Agreement, Orchestra BioMed, Inc. received an upfront payment of $30.0 million in 2019 and an equity commitment of up to $5.0 million of which $2.5 million was invested in June 2019 as part of the Orchestra BioMed, Inc. Series B-1 financing and $2.5 million was invested in June 2022 as part of the Orchestra BioMed, Inc. Series D-2 financing.

Pursuant to the terms of the Terumo Agreement, Orchestra BioMed, Inc. had licensed intellectual property rights to Terumo and the Company was primarily responsible for completing the development of the product in the United States to support premarket approval by the FDA for the ISR indication. These research and development services to be provided by the Company included (i) manufacturing, testing and packaging the drug required for the clinical trials, (ii) supplying Terumo with information related to the design and manufacture of the delivery device and the technology transfer needed for Terumo to ultimately commence manufacture of the delivery device, and (iii) carrying out regulatory activities related to clinical trials in the United States for the ISR indication.

The Company had concluded that the license granted to Terumo was not distinct from the research and development services that were to be provided to Terumo through the completion of the development of ISR indication, as Terumo would not obtain the benefit of the license without the related research and development services. Accordingly, the Company had recognized revenues for this combined performance obligation over the estimated period of research and development services using a proportional performance model. The Company had previously measured proportional performance based on the costs incurred relative to the total estimated costs of the research and development services.

Termination and Right of First Refusal Agreement

On October 24, 2025 (the "Effective Date"), Orchestra BioMed, Inc., entered into a Termination and ROFR Agreement with Terumo, pursuant to which the Terumo Agreement was terminated, and Orchestra BioMed, Inc. agreed to grant Terumo a right of first refusal (the "ROFR") with respect to certain transactions involving Virtue SAB for the treatment of coronary artery disease globally in exchange for a fee of $10.0 million, which was paid on November 7, 2025. The ROFR does not apply to other vascular indications, such as below-the-knee peripheral artery disease, which were covered by the Terumo Agreement prior to its termination. Accordingly, all rights to these indications are fully retained by the Company.

The ROFR has a term that began on the Effective Date and will end on the date that is 90 days after Orchestra BioMed, Inc. discloses primary endpoint data from its U.S. clinical trial for Virtue SAB pursuant to its investigational device exemption ("IDE") for ISR to Terumo or the public, whichever occurs first (the "ROFR Period"); provided, however, that the ROFR Period will immediately expire if Terumo completes the acquisition from a third party of the exclusive right to make, use, sell, offer to sell or distribute a Competing Product (as defined in the Termination and ROFR Agreement) in the United States.

Notice of Third-Party Proposal

The ROFR provides that, in the event that during the ROFR Period, Orchestra BioMed, Inc. receives a written proposal (a "Third-Party Proposal") reflecting the material terms of an agreement pursuant to which Orchestra BioMed, Inc. would grant to a third party either (i) an outright or staged acquisition rights to Virtue SAB or its components or (ii) a license of or the right to distribute Virtue SAB, in each case, in the treatment of coronary artery diseases (a "Virtue Transaction"), Orchestra BioMed, Inc. will promptly deliver notice of each such Third-Party Proposal together with a copy of the applicable Third-Party Proposal to Terumo (a "Third-Party Proposal Notice").

Exercise of ROFR

Pursuant to the Termination and ROFR Agreement, Terumo will have 30 days after delivery of the Third-Party Proposal Notice (the "ROFR Determination Period") to exercise the ROFR by providing written notice to Orchestra BioMed, Inc. (the "ROFR Notice"). In the event that Terumo exercises the ROFR during the ROFR Determination Period, the Company and Terumo will negotiate in good faith and on an exclusive basis during the period beginning on the date of delivery of the ROFR Notice and ending 90 days thereafter (the "Terumo ROFR Negotiation Period") to enter into a Virtue Transaction on substantially the same terms set forth in the applicable Third-Party Proposal.

If Terumo fails to deliver a ROFR Notice to Orchestra BioMed, Inc. prior to the expiration of the ROFR Determination Period, Terumo shall be deemed to have waived the ROFR with respect to the applicable Third-Party Proposal. If Terumo is deemed to have waived a Terumo ROFR pursuant to the preceding sentence, or if Terumo delivers a ROFR Notice within the applicable ROFR Determination Period, but the parties fail to enter into a definitive agreement regarding a Virtue Transaction prior to expiration of the Terumo ROFR Negotiation Period, then, in either case, effective upon such expiration, (i) the ROFR shall terminate, and be of no further force or effect, with respect to the applicable Third-Party Proposal Notice and (ii) Orchestra BioMed, Inc. shall be free to terminate negotiations with Terumo and to enter into a Virtue Transaction with the applicable third party; provided that Orchestra BioMed, Inc. shall not enter into a definitive agreement with the applicable third party on terms and conditions that are materially different than the applicable Third-Party Proposal without first providing Terumo with a renewed Third-Party Proposal Notice and ROFR Determination Period; provided, further, that, if Orchestra BioMed, Inc. does not consummate a transaction with respect to such Third-Party Proposal within 90 days after termination of the ROFR, Terumo will retain its ROFR during the remaining portion of the ROFR Period.

Sale Transaction

In the event that Orchestra BioMed, Inc. receives a written proposal reflecting the material terms of an agreement for a Sale Transaction (as defined in the Termination and ROFR Agreement) of Orchestra BioMed, Inc. (such transaction an "Orchestra Sale"), or if Orchestra BioMed, Inc.'s board of directors approves a formal transaction process for a Orchestra BioMed, Inc. Sale (a "Sale Process"), Orchestra BioMed, Inc. will promptly give Terumo written notice (an "Orchestra Sale Notice"). During the period of 30 days that begins with the delivery of the Orchestra Sale Notice (the "Orchestra Sale Notice Period"), Orchestra BioMed, Inc. will not enter into a binding agreement or other arrangement for an Orchestra Sale with any third party. During the Orchestra Sale Notice Period, Terumo shall be given the opportunity to make an offer with respect to a Virtue Transaction, and Orchestra BioMed, Inc. will consider in good faith any such offer made. In addition, Orchestra BioMed, Inc. shall give Terumo the opportunity to participate in any Sale Process and shall consider any offer by Terumo in connection therewith in good faith.

Term

The Termination and ROFR Agreement will remain in effect for (a) the ROFR Period or (b) the end of any Terumo ROFR Negotiation Period and expiration of the parties rights and obligations under Section 3.2 of the Termination and ROFR Agreement with respect to the exercise of the ROFR, whichever comes later; provided that the Termination and ROFR Agreement will automatically terminate in the event that Orchestra BioMed, Inc. has not disclosed primary endpoint data from a U.S. clinical trial pursuant to its IDE for coronary ISR to Terumo or the public prior to the tenth anniversary of the Effective Date.

In 2019, Orchestra BioMed, Inc. received a total of $32.5 million from Terumo related to the stock purchase and the revenue generating elements of the Terumo Agreement. The Company recorded the estimated fair value of the shares of $2.5 million in stockholders' equity, as the value paid by Terumo is consistent with the value paid by other third-party stockholders in Orchestra BioMed, Inc.'s offering of its Series B-1 Preferred Stock. The Company allocated the remaining $30.0 million, which is non-refundable, to the transaction price of the Terumo Agreement and was recorded to deferred revenue.

The ROFR is concluded to not result in a performance obligation for the Company under ASC 606 and therefore the $10.0 million received was recognized as partnership revenue for the year ended December 31, 2025. Pursuant to the terms of the Termination and ROFR Agreement, Orchestra BioMed, Inc. has no further performance obligations under the Terumo Agreement and therefore recognized the remaining amounts of deferred revenue.

The following table presents the changes in the Company's deferred revenue balance from the Terumo Agreement during the years ended December 31, 2025 and 2024 (in thousands):

Deferred Revenue – January 1, 2024	$	17,433
Revenue recognized		(2,005)
Deferred Revenue – December 31, 2024	$	15,428
Revenue recognized		(15,428)
Deferred Revenue – December 31, 2025	$	—

Series A Preferred Stock

On November 6, 2025, the Company filed a Certificate of Designation of Series A Preferred Stock (the "Certificate of Designation") with the Secretary of State of the State of Delaware. The Certificate of Designation sets forth the rights, preferences, powers, restrictions, and limitations of the Series A Preferred Stock, par value $0.0001 per share ("Series A Preferred Stock"). Below is a summary of certain of the provisions of the Certificate of Designation.

Rank; Liquidation

With respect to distribution of assets upon liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, a holder of Series A Preferred Stock (a "Holder" or, collectively, "Holders") will be entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment is made to the holders of Company Common Stock (or any other class of securities junior to the Series A Preferred Stock) in an amount equal to the liquidation value of the shares of Series A Preferred Stock ("Preferred Shares") held by such Holder. The liquidation value of the Series A Preferred Stock will equal the purchase price of $100.00 per Share (the "Liquidation Value") and will be subject to adjustment for stock splits and the like in accordance with the terms of the Certificate of Designation.

Conversion

Under the terms of the Certificate of Designation, a Holder may convert its Preferred Shares into Company Common Stock on or after the earlier of (i) the date that both (a) the Company has publicly disclosed primary endpoint data from its U.S. IDE study for ISR and (b) the trading price of the Company Common Stock has been above $15.00 per share on any trading day subsequent to such public disclosure or (ii) the consummation of a Change of Control (as defined in the Certificate of Designation). A Holder may convert all or any portion of the outstanding whole Preferred Shares held by such Holder into an aggregate number of shares of Company Common Stock as is determined by (i) multiplying the number of Preferred Shares to be converted by the Liquidation Value thereof, and then (ii) dividing the result by the Conversion Price (as defined below) in effect immediately prior to such conversion, with cash being paid in lieu of fractional shares. The "Conversion Price" for the Series A Preferred Stock will be the greater of (i) $12.00 per share and (ii) a 20% discount to the closing price of the Company Common Stock on the Nasdaq Global Market on the date of conversion. Assuming no adjustments to the Conversion Price or the Liquidation Value as a result of stock splits or similar transactions, the 200,000 Preferred Shares would convert into a maximum of 1,666,666 shares of Company Common Stock.

Redemption at the Option of Holders upon a Change of Control

Upon the occurrence of a Change of Control, subject to limited exceptions, each Holder of Preferred Shares shall have the right to require the Company to redeem all or any part of such Holder's Preferred Shares at a redemption price in cash equal to the aggregate Liquidation Value of such Preferred Shares.

No Voting Rights

Except as otherwise required by the Delaware General Corporation Law, the Holders shall have no voting rights.

Participating Dividends

If the Company declares or pays a dividend or distribution on all shares of the Company Common Stock, whether such dividend or distribution is payable in cash, securities, or other property but excluding any dividend or distribution payable on the Company Common Stock in shares of Company Common Stock, the Company shall simultaneously declare and pay a dividend on the Series A Preferred Stock on a pro rata basis with the Company Common Stock determined on an as-converted basis assuming all Preferred Shares had been converted as of immediately prior to the record date of the applicable dividend (or if no record date is fixed, the date as of which the record holders of Company Common Stock entitled to such dividends are to be determined).

Lockup Agreement

On October 24, 2025, concurrent with the execution of the Termination and ROFR Agreement, the Company and Terumo entered into a Lockup Agreement (the "Lockup Agreement"), pursuant to which Terumo agreed, subject to limited exceptions, that it and its affiliates will not Transfer (as such term is defined in the Lockup Agreement) or enter into any swap, hedging or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of any shares of Company Common Stock held by Terumo until October 24, 2026; provided that the Lockup Agreement only applies to Company Common Stock held by Terumo and its affiliates as of the date of the Lockup Agreement.

The Series A Preferred Stock had a fair market value of $12.6 million as of the issuance date and was recognized as part of mezzanine equity. The remaining $7.4 million of the $20.0 million received in consideration resulted in a premium that was recognized as Partnership revenue for the year ended December 31, 2025.

4. Medtronic Agreement

In June 2022, Orchestra BioMed, Inc., BackBeat and Medtronic entered into the Medtronic Agreement for the development and commercialization of AVIM Therapy for the treatment of pacemaker-indicated patients with uncontrolled HTN despite the use of anti-hypertensive medications (the "Primary Field"). Under the terms of the Medtronic Agreement, the Company is sponsoring an ongoing multinational pivotal study, to support regulatory approval of AVIM Therapy in the Primary Field and is financially responsible for development, clinical and regulatory costs associated with this pivotal study. AVIM Therapy has been integrated into the Medtronic top-of-the-line, commercially available dual-chamber pacemaker system specifically for use in the pivotal trial and will provide development, clinical and regulatory resources in support of the pivotal trial, for which the Company will reimburse Medtronic at cost.

Under the terms of the Medtronic Agreement, Medtronic will have exclusive rights to commercialize AVIM-enabled pacing systems globally following receipt of regulatory approval. Medtronic would be entirely responsible for global commercialization following receipt of regulatory approvals, including manufacturing, sales, marketing and distribution costs.

The Company is expected to receive between $500 and $1,600 per AVIM-enabled device sold based on a formula of the higher of (1) a fixed dollar amount per AVIM-enabled device (amount varies materially on a country-by-country basis) or (2) a percentage of the AVIM Therapy-generated sales. Procedures using the AVIM-enabled pacemakers are expected to be billed under existing reimbursement codes.

Medtronic has a right of first negotiation through FDA approval of AVIM Therapy in the Primary Field, to expand its global rights to AVIM Therapy for the treatment of HTN patients not indicated for a pacemaker.

The Company assessed whether the Medtronic Agreement fell within the scope of ASC 808 and concluded that the Medtronic Agreement is a collaboration within the scope of ASC 808. In addition, the Company determined that Medtronic is a customer for a good or service that is a distinct unit of account, and therefore, the transactions in the Medtronic Agreement should be accounted for under ASC 606.

The Company has concluded that the license granted to Medtronic is not distinct from the development and implementation services that will be provided to Medtronic through the completion of the development of HTN indication, as Medtronic cannot obtain the benefit of the license without the related development and implementation services. ASC 606-10-55-65 includes an exception for the recognition of revenue relating to licenses of intellectual property with sales-based or usage-based royalties. Under this exception, royalty revenue is not recorded until the subsequent sale or usage occurs, or the performance obligation has been satisfied, whichever is later.

The Company concluded that the exemption applies and therefore, the royalty revenue associated with these performance obligations will be recognized as the underlying sales occur. Additionally, pursuant to the Medtronic Agreement, expenses incurred by Medtronic in connection with clinical device development and regulatory activities performed will be reimbursed by the Company. The Company will record such expenses as research and development expenses as incurred. During the years ended December 31, 2025 and 2024, the Company incurred approximately $13.7 million and $9.2 million, respectively, of research and development costs related to these reimbursements pursuant to the Medtronic Agreement, of which $5.3 million and $5.1 million, respectively, is included within accounts payable and accrued expenses in the Company's December 31, 2025 and 2024 consolidated balance sheets.

Concurrently with the close of the Medtronic Agreement, Orchestra BioMed, Inc. also received a $40.0 million investment from Medtronic in connection with Orchestra BioMed, Inc.'s Series D-2 Preferred Stock financing. The equity was purchased at a fair value consistent with the price paid by other investors at that time, and accordingly, the proceeds received were recorded as an equity investment.

On July 31, 2025, Orchestra BioMed, Inc., BackBeat and Medtronic entered into an amendment to the Medtronic Agreement, which became effective on August 4, 2025 (the "Medtronic Agreement Amendment"), to provide, among other things, a development and commercialization framework for future AVIM-therapy integration into a dual-chamber leadless pacemaker. Pursuant to the Medtronic Agreement Amendment, the Company will, among other things, be required to reimburse Medtronic for certain expenses incurred in connection with the integration of AVIM-therapy into Medtronic's dual-chamber leadless pacemaker, up to a specified cap.

On July 31, 2025, the Company and its wholly-owned subsidiaries, Orchestra BioMed, Inc. and BackBeat, entered into a loan agreement with Medtronic, pursuant to which Medtronic agreed to extend a convertible loan to the Company in the aggregate original principal amount of $20.0 million. For additional details, see Note 16 – *"Debt Financing."*

Concurrently with the close of the Medtronic Agreement Amendment on August 4, 2025, Medtronic, through an affiliate, Covidien Group S.à.r.l. ("Covidien"), purchased 4,077,427 shares of Company Common Stock at a purchase price of $2.75 per share, for an aggregate purchase price of approximately $11.2 million, pursuant to a stock purchase agreement, dated as of July 31, 2025 and amended on August 1, 2025, between the Company and Covidien (as amended, the "Medtronic Stock Purchase Agreement"). Pursuant to the terms of the Medtronic Stock Purchase Agreement, Covidien purchased an additional 132,282 shares of Company Common Stock on August 28, 2025 at a purchase price of $2.75 per share, for an aggregate purchase price of $363,775, as a result of the exercise by the underwriters in the Public Offering (as defined below) of their option to purchase an additional 2,182,500 shares of Company Common Stock (See Note 8 – *"Common and Preferred Stock"*). The equity was purchased at a fair value consistent with the price paid by other investors at that time, and accordingly, the proceeds received were recorded as an equity investment.

Through December 31, 2025, there have been no amounts recognized as revenue under the Medtronic Agreement, as amended pursuant to the Medtronic Agreement Amendment (the "Amended Medtronic Agreement").

5. Financial Instruments and Fair Value Measurements

The following tables summarize the Company's financial assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy:

	December 31, 2025			
(in thousands)	**Level 1**	**Level 2**	**Level 3**	**Total**
Assets				
Money market fund (included in Cash and cash equivalents)	$ 12,789	$ —	$ —	$ 12,789
Corporate and government debt securities (included in Marketable securities)	—	71,822	—	71,822
Total assets	**$ 12,789**	**$ 71,822**	**$ —**	**$ 84,611**
Liabilities				
Derivative liability (Note 9)	—	—	2,749	2,749
Total liabilities	**$ —**	**$ —**	**$ 2,749**	**$ 2,749**

	December 31, 2024			
(in thousands)	**Level 1**	**Level 2**	**Level 3**	**Total**
Assets				
Money market fund (included in Cash and cash equivalents)	$ 12,248	$ —	$ —	$ 12,248
Corporate and government debt securities (included in Marketable securities)	—	44,551	—	44,551
Total assets	**$ 12,248**	**$ 44,551**	**$ —**	**$ 56,799**
Liabilities				
Derivative liability	—	—	—	—
Total liabilities	**$ —**	**$ —**	**$ —**	**$ —**

The Level 2 assets consist of government and corporate debt securities which are valued using market observable inputs, including the current interest rate and other characteristics for similar types of investments, whose fair value may not represent actual transactions of identical securities. There were no transfers between Levels 1, 2 or 3 for the periods presented.

Level 3 liabilities consist of the derivative liability associated with the Series A Preferred Stock, of which the fair values were measured upon issuance of the Series A Preferred Stock and are remeasured to fair value at each reporting period. The valuation methodology and underlying assumptions are discussed further in Note 8 – *"Common and Preferred Stock"* and Note 9 – *"Derivative Liabilities."* Significant change to the inputs used in determining the fair value would result in significant changes to the fair value measurement.

6. Marketable Securities and Strategic Investments

Marketable Securities

The following is a summary of the Company's marketable securities as of December 31, 2025 and 2024:

	December 31, 2025			
(in thousands)	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 69,308	$ 60	$ (2)	$ 69,366
Government debt securities	2,454	2	—	2,456
Total	**$ 71,762**	**$ 62**	**$ (2)**	**$ 71,822**

	December 31, 2024			
(in thousands)	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	$ 43,724	$ 57	$ (5)	$ 43,776
Government debt securities	775	—	—	775
Total	**$ 44,499**	**$ 57**	**$ (5)**	**$ 44,551**

The Company believes it is more likely than not that its marketable securities in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. To date, the Company has not recorded any allowance for credit losses on its investment securities. The Company determined that the unrealized losses were not attributed to credit risk but were primarily driven by the broader change in interest rates. As of December 31, 2025, $4.9 million of the Company's marketable securities had maturities of 12 to 36 months while the remaining marketable securities had maturities of less than 12 months.

For the year ended December 31, 2025, the Company did not recognize any realized gains or losses on its marketable securities. For the year ended December 31, 2024, the Company recognized a realized gain on its marketable securities of $11,000.

Strategic Investments

The Company's long-term strategic investments as of December 31, 2025 represent investments made in Vivasure in 2022, 2021 and 2020 that were originally recorded at cost. There were no observable price changes or impairments identified during the years ended December 31, 2025 or 2024 related to these investments. For an update to this investment, see Note 19 – *"Subsequent Events."*

7. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following:

(in thousands)	December 31, 2025	December 31, 2024
Equipment	$ 2,743	$ 2,084
Office furniture	444	444
Leasehold improvements	159	159
Property and equipment, gross	3,346	2,687
Less accumulated depreciation and amortization	(1,631)	(1,303)
Total Property and equipment, net	**$ 1,715**	**$ 1,384**

As of December 31, 2025, $462,000 of equipment is not yet in service and has not yet commenced depreciation. Depreciation and amortization expense was $327,000 and $308,000 for the years ended December 31, 2025 and 2024, respectively.

Accrued Expenses and Other Liabilities

Accrued expenses and other liabilities consist of the following:

(in thousands)	December 31, 2025	December 31, 2024
Clinical trial accruals	$ 4,151	$ 2,893
Accrued compensation	4,160	2,612
Other accrued expenses	1,579	579
Total Accrued expenses and other liabilities	**$ 9,890**	**$ 6,084**

8. Common and Preferred Stock

Common Stock

The Company is authorized to issue up to 340,000,000 shares of Company Common Stock.

Preferred Stock

The Company is authorized to issue 10,000,000 shares of preferred stock with a par value of $0.0001 per share. The board of directors of the Company (the "Board") has the authority to issue preferred stock and to determine the rights, privileges, preferences, restrictions, and voting rights of those shares. As of December 31, 2025, 200,000 shares of preferred stock were outstanding. As of December 31, 2024, no shares of preferred stock were outstanding.

Series A Preferred Stock

On October 24, 2025, concurrent with the execution of the Termination and ROFR Agreement, the Company and TMC entered into a securities purchase agreement (the "Terumo Securities Purchase Agreement"), pursuant to which TMC purchased 200,000 shares of Series A Preferred Stock at a purchase price equal to $100.00 per share for gross proceeds to the Company of $20.0 million. The closing of the sale of the Preferred Shares pursuant to the Terumo Securities Purchase Agreement occurred on November 7, 2025.

The Series A Preferred Stock was accounted for as mezzanine equity in accordance with ASC 480 and the embedded conversion and redemption features were separated from the host instrument and recognized as derivative liability with change in fair value at each reporting period end recognized in the consolidated statements of operations and comprehensive loss. (see Note 9 – *"Derivative Liabilities"*).

The Company utilized an option pricing valuation to determine the fair value of the Series A Preferred Stock at issuance. The valuation incorporated Level 3 inputs in the fair value hierarchy including the expected life of Series A Preferred Stock, expected volatility, and discount rate as well as probability-weighted outcomes. Assumptions used in the valuation also take into account the contractual terms as well as the quoted price of the Company's common stock in an active market. Significant changes in any of these inputs in isolation would result in significant changes to the fair value measurement.

A roll-forward of the Series A Preferred Stock activity is presented below for the year ended December 31, 2025 (in thousands):

	December 31, 2025
Beginning balance, January 1, 2025	**$ —**
Proceeds received pursuant to the issuance of Series A Preferred Stock	20,000
Recognition of fair value of embedded derivatives at issuance (Note 9)	(3,003)
Premium recognized in Partnership revenue	(7,443)
Adjustment to carrying value of Series A Preferred Stock	254
Ending balance, December 31, 2025	**$ 9,808**

Equity Offerings

The Company completed an underwritten public offering and private placements in August 2025. Pursuant to the public offering, (i) on August 4, 2025, the Company sold (a) 9,413,637 shares of Company Common Stock at a price of $2.75 per share and (b) pre-funded warrants to purchase 5,136,363 shares of Company Common Stock at a price to the public of $2.7499 per pre-funded warrant (the "Pre-Funded Warrants"), which represents the per share public offering price for the shares of Company Common Stock less the $0.0001 per share exercise price for each Pre-Funded Warrant and (ii) on August 28, 2025, the Company sold an additional 2,182,500 shares of Company Common Stock pursuant to the underwriters exercise of their option to purchase additional shares (the "Public Offering"). Pursuant to the private placements, (i) on August 4, 2025, the Company sold 5,895,608 shares of Company Common Stock and (ii) on August 28, 2025, the Company sold an additional 132,282 shares of Company Common Stock, in each case, at a price of $2.75 (the "Private Placements"). The total gross proceeds from the Public Offering and the Private Placements were approximately $62.6 million, before deducting underwriting discounts and commissions and offering expenses.

At-the-Market Offering and Shelf Registration Statement

On May 15, 2024, the Company entered into an Open Market Sale Agreement℠ (the "Prior Agreement") with Jefferies LLC ("Jefferies"), pursuant to which the Company could offer and sell, from time to time through Jefferies, up to $100.0 million of shares of Company Common Stock (the "Prior ATM Shares") by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the "Securities Act").

Also on May 15, 2024, the Company filed a shelf registration statement on Form S-3 with the SEC (the "Shelf Registration Statement"), which contains a base prospectus, covering up to a total aggregate offering price of $300.0 million of Company Common Stock, preferred stock, debt securities, warrants, right and/or units, and a prospectus supplement that covered the offering, issuance and sale of the Prior ATM Shares, which are included in the $300.0 million of securities that may be offered, issued and sold by the Company pursuant to the Shelf Registration Statement.

On July 11, 2024, the Company sold 2,000,000 shares of Company Common Stock under the Prior Agreement resulting in aggregate gross proceeds to the Company of approximately $15.5 million and net proceeds to the Company of approximately $15.0 million.

On August 12, 2024, the Company entered into a sales agreement (the "Sales Agreement") with TD Securities (USA) LLC, as agent ("TD Cowen"), pursuant to which the Company may offer and sell, from time to time through TD Cowen, up to $100.0 million of shares of Company Common Stock (the "Offering") by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. The Offering is being made pursuant to the Shelf Registration Statement, filed with the SEC on May 15, 2024 and declared effective on May 24, 2024, a base prospectus, dated May 24, 2024, included as part of the Shelf Registration Statement, and a prospectus supplement, dated August 12, 2024 filed with the SEC pursuant to Rule 424(b)(5) on August 12, 2024.

On November 14, 2025, the Company sold 382,024 shares of Company Common Stock under the Sales Agreement resulting in aggregate gross proceeds to the Company of approximately $1.6 million and net proceeds to the Company of approximately $1.5 million. As of December 31, 2025, the Company had up to $98.4 million of Company Common Stock available to sell under the Sales Agreement.

Termination of Prior Agreement

In connection with the entry into the Sales Agreement, on August 12, 2024, the Company terminated the Prior Agreement between the Company and Jefferies (the "Termination"), in accordance with its terms and with the mutual agreement of Jefferies. The purpose of the Termination was to eliminate restrictions under certain SEC rules relating to the publication or dissemination of new research reports on the Company's business by Jefferies in light of its role as sales agent under the Prior Agreement. The Company had $84.5 million remaining available under the Prior Agreement. The Company cannot make any further sales of Company Common Stock pursuant to the Prior Agreement.

9. Derivative Liability

The Company assessed the Series A Preferred Stock features to determine whether any features are required to be bifurcated and separately accounted for as an embedded derivative. The Company concluded that certain conversion and redemption features meet the requirements to be separately accounted for as a bifurcated derivative. The Series A Preferred Stock was accounted for as mezzanine equity in accordance with ASC 480 and the embedded conversion and redemption features were separated from the host instrument and recognized as derivative liabilities with change in fair value at each reporting period end recognized in the consolidated statements of operations and comprehensive loss.

As of December 31, 2025, the Company remeasured the derivative liability for the Series A Preferred Stock to fair value of $2.7 million. The Company recognized gains of $254,000 for the year ended December 31, 2025 in the change in fair value of derivative liability associated with the Series A Preferred Stock in the consolidated statements of operations and comprehensive loss.

The Company performed a "with-and-without" scenario analysis to determine the fair value of the derivative liability by comparing the value of the Series A Preferred Stock including the bifurcated embedded derivatives to the value of the Series A Preferred Stock excluding them. The Company utilized an option pricing valuation with the expected life of Series A Preferred Stock, expected volatility, and discount rate as significant inputs as well as probability-weighted outcomes. Assumptions used in the valuation also take into account the contractual terms as well as the quoted price of the Company's common stock in an active market. Significant changes in any of those inputs in isolation would result in significant changes to the fair value measurement.

The following table presents changes in Level 3 liabilities measured at fair value for the year ended December 31, 2025 (in thousands):

	December 31, 2025
Derivative liability – January 1, 2025	**$** —
Fair value of embedded derivatives at issuance of Series A Preferred Stock (Note 8)	3,003
Change in the fair value of derivative liability	(254)
Derivative liability – December 31, 2025	**$ 2,749**

The option pricing valuation used to determine the fair value, used the following assumptions:

	November 7, 2025	December 31, 2025
Expected term (in years)	2.15	2.00
Expected volatility	87 %	80 %
Risk-free interest rate	3.51 %	3.41 %
Expected dividend yield	0 %	0 %
Market discount rate	13.10 %	14.79 %
Fair value of common stock	3.81	4.15

Each of these inputs is subjective and generally requires significant judgment and estimation by management:

Expected Term — The expected term represents the estimated time until the conversion or redemption events are achieved.

Expected Volatility — The Company derives volatility over the expected term using its own historical stock price volatility.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of the initial valuation and all thereafter for zero-coupon U.S. Treasury notes with maturities commensurate with the expected term.

Expected Dividend Yield — The expected dividend yield is zero as the Company has not paid, and the Company does not anticipate paying, any dividends on the Company Common Stock in the foreseeable future.

Market Discount Rate – The Company utilizes the S&P corporate yield curve with a tenor commensurate with the expected term to estimate a discount rate applicable to the Company's credit risk.

Fair Value of Common Stock — The Company utilizes the price of its publicly-traded Company Common Stock as an input in determining the fair value of the derivative.

10. Warrants

The Company evaluates its outstanding warrants to determine if the instruments qualify for equity or liability classification.

Summarized Outstanding Warrants

The following table summarizes outstanding warrants to purchase shares of Company Common Stock as of December 31, 2025 and 2024:

	Number of Shares			
	December 31, 2025	December 31, 2024	Exercise Price	Expected Term
Equity-classified Warrants				
Pre-Funded Warrants[1]	5,136,363	—	$0.0001	N/A
Ligand Warrants (Note 15)[2]	2,000,000	—	$3.67	5.16
Orchestra BioMed, Inc. Warrants	507,841	507,841	$1.08 – $30.11	0.10 – 8.75
Hercules Warrants (Note 16)	167,598	52,264	$3.58 – $5.74	3.13 – 3.50
Avenue Warrants	27,707	27,707	$7.67	2.50
Non-employee Warrants (Note 11)	60,000	—	$4.69	2.84
Private Warrants Held by Sponsor[3]	750,000	750,000	$11.50	4.32 – 4.57
Officer and Director Warrants[4]	635,000	660,000	$11.50	4.32
Total Outstanding	9,284,509	1,997,812		

(1) In August 2025, the Company received $2.7499 per the Pre-Funded Warrant issued, or $14.1 million in aggregate proceeds. Each Pre-Funded Warrant may be exercised for $0.0001 per Pre-Funded Warrant (see Note 8).

(2) Represents warrants initially issued by Orchestra BioMed, Inc., which converted into warrants to acquire Company Common Stock in connection with the Business Combination (the "Orchestra BioMed, Inc. Warrants").

(3) The Sponsor purchased 1,500,000 warrants to purchase shares of HSAC2 in a private placement upon consummation of the HSAC2 initial public offering (the "Private Warrants"), 750,000 of which were forfeited by the Sponsor immediately prior to the closing of the Business Combination (the "Sponsor Forfeiture").

(4) Pursuant to the terms of the Business Combination, immediately following the Sponsor Forfeiture and prior to the closing of the Business Combination, HSAC2 issued 750,000 warrants to purchase Company Common Stock to eleven specified employees and directors of Orchestra (the "Officer and Director Warrants"). These Officer and Director Warrants have substantially similar terms to the forfeited Private Warrants, except they were subject to vesting provisions that expired in January 2026. There are fewer than 750,000 Officer and Director Warrants outstanding currently due to forfeitures by persons that resigned from the Company prior to the vesting of the Officer and Director Warrants.

11. Stock-Based Compensation

Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan

On January 26, 2023, the Company adopted the 2023 Plan which permits the granting of incentive stock options, non-qualified options, stock appreciation rights, restricted stock, restricted stock units, performance awards and other stock-based award to employees, directors, and non-employee consultants and/or advisors. As of December 31, 2025, 377,306 remaining shares of Company Common Stock were authorized for issuance pursuant to awards under the 2023 Plan. The pool of available shares will be automatically increased on the first day of each calendar year, beginning January 1, 2024 and ending January 1, 2032, by an amount equal to the lesser of (i) 4.8% of the outstanding shares of the Company Common Stock determined on a fully-diluted basis as of the immediately preceding December 31 and (ii) 3,036,722 shares of Company Common Stock, and (iii) such number of shares of Company Common Stock determined by the Board or the Compensation Committee prior to January 1st of a given year. Employees, consultants, and directors are eligible for awards granted under the 2023 Plan, which generally have a contractual life of up to 10 years and may be exercisable in cash or as otherwise determined by the Board. Vesting generally occurs over a period of not greater than four years.

Orchestra BioMed Holdings, Inc. 2025 New Hire Inducement Plan

In November 2025, the Company's Board of Directors adopted the 2025 New Hire Inducement Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of nonstatutory stock options, stock appreciation rights, restricted stock, RSUs and other stock-based awards with respect to an aggregate of 950,000 shares of Company Common Stock (subject to adjustment as provided in the Inducement Plan). Awards under the Inducement Plan may only be granted to new employees who were not previously an employee or director of the Company or are commencing employment with the Company following a bona fide period of non-employment, in either case, as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4). In November 2025, the Company granted inducement equity awards to twelve new employees as a material inducement to acceptance of their respective employment consisting of stock options to purchase up to an aggregate of 151,250 shares of the Company Common Stock. As of December 31, 2025, there were 798,750 shares remaining available for future issuance under the Inducement Plan.

Stock-based Compensation Expense

Total stock-based compensation related to option issuances was as follows:

	Year Ended December 31,	
(in thousands)	**2025**	**2024**
Research and development	$ 2,290	$ 1,835
Selling, general and administrative	2,131	2,523
Total stock-based compensation	**$ 4,421**	**$ 4,358**

As of December 31, 2025, there was approximately $6.6 million of unrecognized stock-based compensation expense associated with the stock options noted above that is expected to be recognized over a weighted average period of approximately 2.7 years.

Total stock-based compensation related to restricted stock awards and restricted stock units was as follows:

	Year Ended December 31,	
(in thousands)	**2025**	**2024**
Research and development	$ 2,131	$ 1,325
Selling, general and administrative	4,299	3,873
Total stock-based compensation	**$ 6,430**	**$ 5,198**

As of December 31, 2025, there was approximately $6.6 million of unrecognized stock-based compensation expense associated with the restricted stock units noted above that is expected to be recognized over a weighted average period of approximately 2.0 years.

On February 28, 2025, the Company issued equity-classified warrants to purchase 60,000 shares of Company Common Stock at an exercise price of $4.69 per share to non-employee consultants. The warrants were issued as consideration for entering into an agreement for future services. At the grant date, 6,000 became exercisable while the remaining vested ratably over eight months. Assumptions used were an expected term (in years) of 2.84, expected volatility of 110.1%, risk-free interest rate of 3.99%, expected dividend yield of 0%, and the fair value of Company Common Stock of $3.12.

Total stock-based compensation related to warrants was as follows:

	Year Ended December 31,	
(in thousands)	**2025**	**2024**
Research and development	$ 364	$ 482
Selling, general and administrative	763	577
Total stock-based compensation	**$ 1,127**	**$ 1,059**

As of December 31, 2025, there was approximately $74,000 of unrecognized stock-based compensation expense associated with the warrants noted above that is expected to be recognized over a weighted average period of approximately 0.1 years.

Stock Option Activity

The following table summarizes the stock option activity of the Company under the 2023 Plan and the Inducement Plan:

	Shares Underlying Options	Weighted Average Exercise Price	Weighted Average Remaining Term (years)	Aggregate Intrinsic Value (000s)
Outstanding at January 1, 2025	5,696,845	$ 7.17	7.39	$ 3
Granted	1,816,774	3.20	—	—
Exercised	(28,251)	4.41	—	33
Forfeited/canceled	(285,797)	5.78	—	—
Outstanding December 31, 2025	**7,199,571**	**$ 6.23**	**7.08**	**$ 1,963**
Exercisable at December 31, 2025	**4,414,171**	**$ 7.50**	**5.92**	**$ 21**

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2025 and 2024 was $2.24 and $3.79 per share, respectively.

Restricted Equity Awards Activity

The following table summarizes the restricted stock awards and restricted stock units activity of the Company under the 2023 Plan:

	Restricted Stock Awards/Units Outstanding	Weighted Average Grant Date Fair Value
Outstanding at January 1, 2025	2,094,584	$ 6.54
Granted	1,455,395	2.72
Vested	(1,211,341)	6.94
Forfeited/canceled	(37,987)	4.58
Outstanding December 31, 2025	2,300,651	$ 3.95

No performance-based restricted stock awards or units were granted in the year ended December 31, 2025. The fair value of restricted stock units vested during the year ended December 31, 2025 was $4.3 million.

Determination of Stock Option Awards Fair Value

The estimated grant-date fair value of all the Company's option awards was calculated using the Black-Scholes option pricing model, based on the following weighted average assumptions:

	Year Ended December 31,	
	2025	2024
Expected term (in years)	6.02	6.15
Expected volatility	81 %	73 %
Risk-free interest rate	3.90 %	4.30 %
Expected dividend yield	0 %	0 %
Fair value of common stock	3.20	5.57

The fair value of each stock option grant was determined by the Company using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

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

Expected Volatility — The Company lacks sufficient company-specific historical and implied volatility information. Therefore, it derives expected stock volatility using a weighted average blend of historical volatility of comparable peer public companies and its own historical volatility, over a period equivalent to the expected term of the stock-based awards.

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

Expected Dividend Yield — The expected dividend yield is zero as the Company has not paid, and the Company does not anticipate paying, any dividends on the Company Common Stock in the foreseeable future.

Fair Value of Common Stock — The Company utilizes the price of its publicly-traded Company Common Stock to determine the grant date fair value of awards.

12. Leases

Office Lease

In August 2024, the Company entered into an additional addendum to the lease agreement for office space in New Hope, PA originally entered into by Orchestra BioMed, Inc. in December 2009 (as amended, the "New Hope Lease"). The New Hope Lease covers 8,052 square feet and will expire in September 2027. Monthly fees under the New Hope Lease will be between $17,000 and $19,000 for the period from the August 2024 addendum through expiration.

In November 2019, Orchestra BioMed, Inc. entered into a new lease agreement for approximately 5,200 square feet of office space in New York, NY. In November 2022, Orchestra BioMed, Inc. entered into an amendment for this lease which increased the office space square footage to approximately 7,800 and amended the expiration to April 2028. Monthly fees will be between $28,000 and $40,000 for the period from commencement through expiration.

In September 2024, the Company entered into a new lease for 6,496 square feet of office space in Fort Lauderdale, Florida. The agreement will expire in December 2027. The monthly fees commenced in November 2024, the commencement date of the agreement, and will be between $16,000 and $17,000 for the period from commencement through expiration.

Operating cash flow supplemental information for the year ended December 31, 2025:

Cash paid for amounts included in the present value of operating lease liabilities was $744,000 during the years ended December 31, 2025 compared to $890,000 during the year ended December 31, 2024.

As of December 31, 2025:	
Weighted average remaining lease term – operating leases, in years	2.14
Weighted average discount rate – operating leases	9.92 %

Operating Leases

Rent/lease expense for office and lab space was approximately $1.0 million and $933,000 for the years ended December 31, 2025 and 2024, respectively. Rent/lease expense includes amounts related to short term leases of $240,000 and $118,000 for the years ended December 31, 2025 and 2024, respectively. Variable lease costs were $104,000 and $163,000 for the years ended December 31, 2025 and 2024, respectively. Variable lease costs consist primarily of common area maintenance costs, insurance and taxes which are paid based upon actual costs incurred by the lessor. The table below shows the future minimum rental payments, exclusive of taxes, insurance, and other costs, under the leases as of December 31, 2025:

Year ending December 31:	Operating Leases (in thousands)
2026	$ 881
2027	829
2028	158
2029	—
2030	—
Thereafter	—
Total future minimum lease payments	$ 1,868
Imputed interest	(181)
Total liability	**$ 1,687**

13. Income Taxes

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred tax assets relate primarily to its net operating loss carryforwards and other balance sheet basis differences. In accordance with ASC 740, *Income Taxes*, the Company recorded a valuation allowance to fully offset the gross deferred tax asset, because it is not more likely than not that the Company will realize future benefits associated with these deferred tax assets at December 31, 2025 and 2024.

The change in the valuation allowance for the years ended December 31, 2025 and 2024 was an increase of $14.4 million and $33.8 million, respectively. Approximately $20.1 million of the increase in 2024 relates to opening balance sheet adjustments related to the Company's asset acquisition.

In general, the U.S. Federal and state income tax returns remain open to examination by taxing authorities for tax years beginning in 2020 to present. However, if the Company claims net operating loss ("NOL") carryforwards from years prior to 2020 against future taxable income, the tax returns pertaining to those losses may be examined by the taxing authorities. The Company's foreign net operating loss carryovers statute of limitations is approximately 4 years.

The components of the deferred tax assets are as follows:

(in thousands)	December 31, 2025	December 31, 2024
Deferred tax assets		
Net operating loss carryovers – Federal	$ 43,123	$ 37,381
Net operating loss carryovers – State	6,686	7,500
Net operating loss carryovers – Foreign	23,171	20,087
Capital loss carryforward	2,885	2,890
Depreciation and amortization	150	180
Unrealized loss on equity securities	—	—
Research and development credits	8,817	6,428
Loss on impairment of strategic investments	1,097	1,098
Research and experimental costs	10,703	12,050
Other	3,311	2,142
Lease liability	443	597
Deferred revenue	8,278	4,118
Total deferred tax assets	108,664	94,471
Less: valuation allowance	(108,271)	(93,910)
Total deferred tax assets	393	561
Deferred tax liabilities		
Right-of-use asset	(393)	(561)
Depreciation and amortization	—	—
Total deferred tax liabilities	(393)	(561)
Total net deferred tax asset	$ —	$ —

A reconciliation of the provision for income taxes to the amount computed by applying the 21% statutory U.S. federal income tax rate to income before income taxes after the adoption of ASU 2023-09 is as follows:

	December 31, 2025	
	In Thousands	Percent
U.S. federal statutory tax rate	$ (11,067)	21.0 %
State and local income tax (net of Federal benefit)	—	— %
Foreign tax effects	—	— %
Effect of changes in tax laws or rates enacted in the current period	—	— %
Effect of cross-border tax laws	—	— %
Tax Credits		
Research and development tax credits	(2,807)	5.3 %
Changes in valuation allowances	11,718	(22.2)%
Nontaxable or nondeductible items		
Stock options	1,093	(2.1)%
162(m)	488	(0.9)%
Other	14	— %
Changes in unrecognized tax benefits	561	(1.1)%
Other	—	— %
Effective tax rate	—	— %

	December 31, 2024
Income tax benefit at federal statutory rate	21.0 %
State and local income tax (net of Federal benefit)	3.8 %
Permanent items	(0.2)%
Research and development credits	2.8 %
Research and development, uncertain tax positions	(0.6)%
Change in valuation allowance	(22.2)%
Effect of rate changes	(0.8)%
Sec 162(m)	(3.6)%
Other	(0.2)%
Effective tax rate	— %

The Company had approximately $205.4 million and $166.6 million of gross NOL carryforwards (federal and state, respectively) and approximately $8.8 million of federal research and development tax credits, respectively, as of December 31, 2025, after applying Section 382 and Section 383 limitations. The federal net operating losses for years ending on or before December 31, 2017 start to expire from 2027 to 2037. The federal net operating losses generated after the year ended December 31, 2017 have an indefinite carryforward period, subject to 80% taxable income limitation on an annual basis. Certain state net operating losses start to expire in 2027, and certain states have an indefinite carryforward period. The federal research and development ("R&D") tax credit starts to expire from 2028 to 2045. As of December 31, 2025, we had approximately $100.7 million of gross foreign NOLs. These losses can be carried forward indefinitely.

The federal and state NOL carryforwards and R&D tax credits are available to reduce future taxable income. However, Sections 382 and 383 of the Internal Revenue Code, and similar state regulations, contain provisions that may limit the NOL carryforwards and R&D tax credits available to be used to offset income in any given year upon the occurrence of certain events, including changes in the ownership interests of significant stockholders. In the event of a cumulative change in the ownership interest of significant stockholders in excess of 50% over a three-year period, the amount of the NOL carryforwards and R&D tax credits that the Company may utilize in any one year may be limited. In 2019, the Company completed Section 382 and Section 383 studies. As a result of these studies, the federal net operating loss and federal R&D tax credit carryforwards were reduced to reflect the amounts that are estimated to not be limited under the provisions of Sections 382 and 383. In 2023 and 2025, the Company performed an updated analysis of the impact of ownership changes on federal net operating loss carryforwards and R&D tax credits for Sections 382 and 383 and determined no adjustments were required to previously recorded limitation amounts.

The Tax Cuts and Jobs Act resulted in significant changes to the treatment of research and experimental expenditures under Section 174. For tax years beginning after December 31, 2021, taxpayers are required to capitalize and amortize these expenditures that are paid or incurred in connection with their trade or business. Specifically, costs for U.S.-based research and experimental activities must be amortized over five years and costs for foreign research and experimental activities must be amortized over 15 years—both using a midyear convention. On July 4, 2025, the President of the U.S. signed into law the One Big Beautiful Bill Act ("OBBBA"), which makes permanent many of the beneficial expired and expiring provisions originally enacted in the Tax Cuts and Jobs Act of 2017, including immediate expensing of domestic research and development expenditures. As of the years ended December 31, 2025 and 2024, the Company recorded a deferred tax asset of $10.7 million and $12.1 million, respectively, for such costs. The effect of the OBBBA did not have a material impact on the effective tax rate in our consolidated financial statements as of December 31, 2025.

In assessing the realizability of the net deferred tax asset, the Company considers all relevant positive and negative evidence in determining whether it is more likely than not that some portion or all of the deferred income tax assets will not be realized. The realization of the gross deferred tax assets is dependent on several factors, including the generation of sufficient taxable income prior to the expiration of the net operating loss carryforwards. Management believes it is more likely than not that the Company's deferred income tax assets will not be realized. As such, the Company has provided a 100% valuation allowance on its net deferred tax assets as of December 31, 2025 and 2024.

Following is a reconciliation of beginning and ending balances of total amounts of gross unrecognized tax benefits.

(in thousands)	December 31, 2025	2024
Unrecognized tax benefits		
Unrecognized tax benefits at the beginning of the period	$ 1,558	$ 1,217
Additions due to current year activity	561	341
Unrecognized tax benefits at the end of the period	$ 2,119	$ 1,558

The total liabilities associated with the unrecognized tax benefits that, if recognized, would impact the Company's effective tax rate were $2.1 million and $1.6 million at December 31, 2025 and 2024, respectively. It is not anticipated that the balance of unrecognized tax benefits at December 31, 2025 will change significantly over the next twelve months. The balance of unrecognized tax benefits as reflected in the table above are recorded on the balance sheet as a reduction to the related deferred tax asset in accordance with ASU 2013-11.

The Company's policy is to recognize interest accrued and, if applicable, penalties related to unrecognized tax benefits in income tax expense for all periods presented. No interest or penalties were recognized during 2025 or 2024.

14. Related Party Transactions

In addition to transactions and balances related to cash and stock-based compensation to officers and directors, the Company had the following transactions and balances with related parties during the years ended December 31, 2025 and 2024:

As part of the Public Offering, on August 4, 2025, (i) entities associated with RTW Investments, LP (collectively, "RTW"), which beneficially owned approximately 21% of the Company Common Stock immediately prior to the Public Offering, purchased Pre-Funded Warrants exercisable for 3,636,363 shares of Company Common Stock and (ii) Perceptive Life Sciences Master Fund, Ltd, which beneficially owned approximately 12% of the Company Common Stock immediately prior to the Public Offering, purchased Pre-Funded Warrants exercisable for 1,500,000 shares of Company Common Stock.

In addition, transactions between the Company and Medtronic are disclosed in both Note 4 – *"Medtronic Agreement"* and Note 16 – *"Debt Financing."*

15. Royalty Purchase Agreement

On July 31, 2025, the Company entered into a revenue participation right purchase and sale agreement (the "Royalty Purchase Agreement") with Ligand. Under the terms of the Royalty Purchase Agreement, in exchange for payment of $35.0 million (the "Investment Amount"), less certain reimbursable expenses, Ligand acquired from the Company the right to receive tiered royalty payments (the "Royalty Interest") with respect to revenue (including certain licensing revenue) received by the Company in a calendar year in connection with worldwide net product sales, or other product revenue received, by the Company and its licensees ("Annual Net Sales") of (a) AVIM Therapy (the "Primary Product") and (b) Virtue SAB (the "Secondary Product" and together with the Primary Product, the "Products") in the field of coronary artery treatment.

Pursuant to the Royalty Purchase Agreement, the Investment Amount shall be paid in two tranches: (i) $20.0 million was paid on August 4, 2025 (the "Ligand Closing") and (ii) $15.0 million is payable on May 1, 2026 (the "Second Installment"), provided certain conditions have been met. In repayment of the Investment Amount, the Company will remit 17.0% of revenues related to the Products until an annual total of $17.0 million has been remitted to Ligand, thereafter the Company will remit (a) 4.0% of revenues related to the Primary Product in the field of hypertension treatment and (b) 4.0% of revenues related to the Secondary Product in the field of coronary artery treatment. In addition, under the terms of the Royalty Purchase Agreement, unless and until Ligand pays the Second Installment, Ligand shall only be entitled to 57.1% of the amounts it would otherwise be due under the Royalty Purchase Agreement. However, regardless of whether the Second Installment has been paid, under the terms of the Royalty Purchase Agreement, the percentages referenced in the second sentence of this paragraph will incrementally increase from 17.0% and 4.0% up to 20.0% and 7.0%, respectively, if the Company does not achieve certain enrollment milestones relating to the BACKBEAT clinical study through January 1, 2027.

The Royalty Interest in respect of Annual Net Sales of the Products will end on the date in which no Product is being developed or commercialized by or on behalf of the Company, any of its affiliates, or any of its or their licensees or distributors and Ligand has received the last Royalty Interest payment payable under the terms of the Royalty Purchase Agreement. The obligations arising under the Royalty Purchase Agreement are secured by security interests in, and pledges over, the Royalty Interest, the Revenue Participation Right (as defined in the Royalty Purchase Agreement) and the Company's interests in the Products and associated intellectual property rights, subject to certain agreed security principles, permitted liens and other customary exceptions and qualifications, and the security interests in the Products and associated intellectual property rights of the Company are subordinate in right of payment to the prior payment in full of the outstanding indebtedness under the 2024 LSA (as defined below). The Royalty Purchase Agreement contains customary representations, warranties and indemnities of the Company and Ligand, and customary covenants on the part of the Company.

In connection with the sale of the Royalty Interest, and pursuant to the terms of the Royalty Purchase Agreement, on August 4, 2025, the Company issued to Ligand the Ligand Warrants to purchase up to 2,000,000 shares of the Company Common Stock (the "Ligand Warrant Shares"), at an exercise price equal to $3.67 per share. The exercise price of the Ligand Warrants and the number of Ligand Warrant Shares issuable upon exercise of the Ligand Warrants are subject to adjustments for stock splits, combinations, stock dividends or similar events. Pursuant to the terms of the Ligand Warrant, the Ligand Warrant Shares shall vest and become exercisable as follows: (i) 1,142,857 of the Ligand Warrant Shares (the "First Tranche") vested upon issuance; and (ii) 857,143 of the Ligand Warrant Shares will vest on the date of payment of the Second Installment. In the event that the Second Installment is not paid, the Ligand Warrant shall only be exercisable with respect to the First Tranche. The Ligand Warrants are exercisable for ten years from the date of issuance.

The Company accounted for its sale of royalty revenues to Ligand, pursuant to the Royalty Purchase Agreement, in accordance with ASC 470, *Debt*, which addresses situations in which an entity receives cash from an investor in return for an agreement to pay the investor a specified percentage of the revenue from a contractual right. The Company classified the proceeds received from the sale to Ligand as debt as the Company determined that it had significant continuing involvement in the generation of the cash flows to Ligand. Interest related to the Royalty Purchase Agreement will be recognized utilizing the effective interest method over the estimated term. When the Company receives the Second Installment, such Second Installment will also be recorded as a liability related to the sale of future royalties when they are received and amortized under the effective interest method over the estimated remaining term of the Royalty Purchase Agreement.

As of the Ligand Closing, the Company's estimate of this total interest expense associated with the Royalty Interest resulted in an effective annual interest rate of approximately 23.1%. This estimate contains significant assumptions that impact the interest expense that will be recognized over the royalty period. The Company will periodically assess the estimated amounts due and payable to Ligand and to the extent that the amount or timing of such payments is materially different than the original estimates, an adjustment will be recorded prospectively to the consolidated statements of operations and comprehensive loss. There are a number of factors that could materially affect the amount and timing of the royalty payments to be paid by the Company to Ligand and, correspondingly, the amount of interest expense recorded by the Company.

The following table shows the activity of the Royalty Purchase Agreement since the transaction inception through the period indicated (in thousands):

	December 31, 2025
Upfront payment from the royalty purchase agreement	$ 20,000
Fair value of warrants	(3,480)
Deferred financing costs	(1,114)
Non-cash interest expense on liability	2,048
Payments	(972)
Royalty purchase agreement	$ 16,482

16. Debt Financing

2025 Medtronic Loan Agreement

On July 31, 2025, the Company and its wholly-owned subsidiaries, Orchestra BioMed, Inc. and BackBeat, entered into a Loan Agreement (the "Medtronic Loan Agreement") with Medtronic, pursuant to which Medtronic agreed to extend a convertible loan to the Company in the aggregate original principal amount of $20.0 million (the "Medtronic Loan"). The Medtronic Loan is evidenced by a secured subordinated convertible promissory note (the "Medtronic Note") of the Company. The issuance of the Medtronic Note to Medtronic and the funding of the Medtronic Loan will take place on April 27, 2026 subject to certain customary closing conditions as described in the Medtronic Loan Agreement.

The Medtronic Note will accrue simple interest at a rate of 11% per annum provided that no interest payments will be paid or due until maturity. The Medtronic Note does not allow for prepayment without the prior consent of Medtronic. Unless earlier converted, or redeemed, the Medtronic Note will mature on April 27, 2031 (the "Repayment Date"). In addition, the payment or other satisfaction of the obligations set forth in the Medtronic Loan Agreement are subordinate in right of payment to the prior payment in full of the senior obligations. The obligations arising under the Medtronic Loan Agreement and the Medtronic Note are secured by security interests in, and pledges over, the Company's assets, subject to certain agreed security principles, permitted liens and other customary exceptions and qualifications.

The principal balance of the Medtronic Note, together with all accrued and unpaid interest thereon (collectively, the "Balance") will automatically convert into a revenue share (the "Revenue Share Credit"), if FDA approval of a Medtronic device incorporating AVIM is achieved prior to the Repayment Date. Upon conversion of the then outstanding Balance the Company shall pay to Medtronic the Revenue Share Credit, which shall equal 15% of the revenue share amounts that the Company receives under the Amended Medtronic Agreement, until such time as the total Revenue Share Credit payments equal $40.0 million.

The Medtronic Loan Agreement contains customary representations, warranties and affirmative and negative covenants. In addition, the Medtronic Loan Agreement contains customary events of default that entitle Medtronic to cause the Company's indebtedness under the Note to become immediately due and payable, and to exercise remedies against the Company and the collateral securing the Loan. Upon the occurrence and for the duration of an event of default, an additional default interest rate equal to 2.0% per annum may apply to all obligations owed under the Loan Agreement.

The proceeds from the Medtronic Loan Agreement have not yet been received so they are not included in the principal payments table below nor included in the consolidated balance sheets.

2024 Loan and Security Agreement

On November 6, 2024 (the "LSA Closing Date"), the Company and certain of its subsidiaries (together with the Company, the "Borrower") entered into a Loan and Security Agreement, by and among the Borrower, the several banks and other financial institutions or entities party thereto, as lenders (collectively, the "Hercules Lenders"), and Hercules Capital, Inc., ("Hercules"), as administrative agent and collateral agent for itself and the Hercules Lenders, as amended by that certain First Amendment to Loan and Security Agreement dated as of December 30, 2024 and Second Amendment (as defined below) dated as of July 31, 2025 (as amended, the "2024 LSA"). Prior to July 31, 2025, the 2024 LSA provided a secured term loan facility of up to $50.0 million available in up to four tranches (collectively, the "Term Loans"), with the first tranche of $15.0 million drawn on the LSA Closing Date, and a second and third tranche of up to an aggregate of $15.0 million available upon achievement of certain performance and financing milestones. Additionally, the Company had access to a fourth tranche of $20.0 million at the discretion of the lender's investment committee.

On July 31, 2025, the Borrower, the Hercules Lenders and Hercules entered into the Second Amendment to the 2024 LSA (the "Second Amendment"), which, among other things, amended the existing 2024 LSA to (i) delay the initial date upon which the Company has to begin amortizing term loans under the 2024 LSA from (a) December 1, 2026 (with amortization payments delayed to as late as December 1, 2027 if certain conditions were met) to (b) July 1, 2027 (with amortization payments delayed to as late as January 1, 2028 if certain conditions are met); (ii) increase by $15.0 million (from $20.0 million to $35.0 million) the amount that that may be borrowed by the Company in the discretion of the lender's investment committee and (iii) eliminate the Company's ability to draw up to $15.0 million if certain milestones are achieved. The Second Amendment became effective on August 4, 2025.

The Term Loans accrue interest at a floating per annum rate equal to the greater of (i) (x) the "prime rate" as reported in The Wall Street Journal plus (y) 2.0%, and (ii) 9.50%. The repayment terms of the Term Loans include monthly payments over a 4-year period, consisting of an interest-only period expiring July 1, 2027, followed by 18 monthly principal payments plus interest, although the interest-only period can be extended for six months under certain circumstances set forth in the 2024 LSA. At the Company's option, the Company may prepay all or a portion of the outstanding Term Loans, subject to a prepayment premium equal to (a) 3.0% of the Term Loans being prepaid if the prepayment occurs during the twelve months following the LSA Closing Date, (b) 2.0% of the Term Loans being prepaid if the prepayment occurs after 12 months following the LSA Closing Date but on or prior to 24 months following the LSA Closing Date, and (c) 1.0% of the Term Loans being prepaid if the prepayment occurs after 24 months following the LSA Closing Date and prior to the maturity date. In addition, the Company will pay an end of term charge of 6.35% of the principal amount of the Term Loans upon the prepayment or repayment of the Term Loans and a facility charge of 0.75% upon any draws of the Term Loans.

In connection with the entry into the 2024 LSA, on the LSA Closing Date, the Company issued each of the Hercules Lenders a warrant to purchase Company Common Stock, which warrants were amended effective August 4, 2025 in connection with the Second Amendment (as amended, each a "Hercules Warrant" and, collectively, the "Hercules Warrants"). Pursuant to the terms of the Hercules Warrants, each Hercules Lender could purchase that number of shares of Company Common Stock equal to (i)(x) 0.04, multiplied by (y) the aggregate principal amount of all Term Loan Advances (as defined in the 2024 LSA) made to the Company by the applicable Lender, divided by (ii) $3.58, which is the exercise price of the Hercules Warrants. Each Hercules Warrant is exercisable for seven years from the LSA Closing Date.

The 2024 LSA includes customary affirmative and negative covenants and representations and warranties, including a covenant against the occurrence of a "change in control," financial reporting obligations, and certain limitations on indebtedness, liens, investments, distributions (including dividends), collateral, transfers, mergers or acquisitions, taxes, corporate changes, and bank accounts. The 2024 LSA also includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that could reasonably be expected to have a "material adverse effect" as set forth in the 2024 LSA, cross acceleration to third-party indebtedness and certain events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, Hercules may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Amended 2024 LSA.

The Company must maintain Qualified Cash (as defined in the 2024 LSA), beginning on December 1, 2025, in an amount greater than or equal to (x) the outstanding principal amount of the Term Loan Advances, multiplied by (y) the applicable Cash Coverage Percentage (as defined in the Second Amendment), which percentage ranges from a minimum of 60% to a maximum of 100% of Term Loan Advances, depending upon the amount of Qualified Cash.

The following table shows the amount of principal payments due pursuant to the Term Loans by year:

Year ending December 31:	Principal Payments (in thousands)
2026	$ —
2027	5,056
2028	9,944
2029	—
Total	**$ 15,000**

Total interest expense recorded on these facilities during the year ended December 31, 2025 and December 31, 2024 was approximately $1.9 million and $297,000, respectively.

17. Segment Disclosures

The Company has one reportable segment, which consists of the development of clinical and preclinical product candidates through risk-reward sharing partnerships with leading medical device companies. The Company's CODM, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of assessing performance and allocating resources based on net loss that also is reported on the consolidated statement of operations and comprehensive loss as consolidated net loss. Net loss is used by the CODM to make key strategic and operational decisions. The measure of segment assets is reported on the consolidated balance sheets as total consolidated assets. The majority of the Company's long-lived assets are held in the United States.

The following table presents selected financial information, including significant expenses regularly reviewed by the CODM, about the Company's single operating segment for the years ended December 31, 2025 and 2024:

	Year Ended December 31,	
	2025	2024
(in thousands)		
Partnership revenue	$ 32,871	$ 2,005
Product revenue	611	633
Expenses:		
Cost of product revenues	190	204
Non-clinical development costs	17,979	15,179
Clinical development costs	12,945	8,079
Personnel and consulting costs	30,028	22,604
Stock-based compensation	11,978	10,615
Depreciation and amortization expense	327	308
Other segment expenses[(1)]	11,588	10,029
Interest expense (income), net	1,148	(3,356)
Net loss	$ (52,701)	$ (61,024)

[1]Other segment expenses primarily include general and administrative costs not presented in other line items.

18. Net Loss Per Share

Basic net loss per share of Company Common Stock is computed by dividing net loss less the adjustment to carrying value of Series A Preferred Stock by the weighted-average number of shares of Company Common Stock which includes the weighted average effect of the Pre-Funded Warrants, for the purchase of shares of common stock, for which the remaining unfunded exercise price is $0.0001 per share. Shares of Company Common Stock outstanding but subject to forfeiture and cancellation by the Company are excluded from the weighted-average number of shares until the period in which such shares are no longer subject to forfeiture. In connection with the Business Combination, the Sponsor agreed that 25% or 1,000,000 of the shares of Company Common Stock held by the Sponsor (the "Forfeitable Shares") will be forfeited to the Company on the first business day following the fifth anniversary of the closing of the Business Combination, unless, as to 500,000 shares, the volume-weighted average price of the Company Common Stock is greater than or equal to $15.00 per share over any 20 trading days within any 30 trading day period (the "Initial Milestone Event"), and as to the remaining 500,000 shares, the volume-weighted average price of the Company Common Stock is greater than or equal to $20.00 per share over any 20 trading days within any 30 trading day period (the "Final Milestone Event"). On April 12, 2023, the Initial Milestone Event was achieved and 500,000 of the Forfeitable Shares are no longer subject to forfeiture. However, the Final Milestone event has not occurred, and 500,000 Forfeitable Shares remain subject to forfeiture.

In connection with the Business Combination, existing Orchestra BioMed, Inc. stockholders had the opportunity to elect to participate in an earnout (the "Earnout") pursuant to which such each electing stockholder (each, an "Earnout Participant") may receive a portion of additional contingent consideration of up to 8,000,000 shares of Company Common Stock (the "Earnout Consideration"). Each Earnout Participant agreed to extend their applicable lock-up period from 6 months to 12 months after the Closing, pursuant to an Earnout Election Agreement and such Earnout Participants are collectively be entitled to receive: (i) 4,000,000 shares of the Earnout Consideration, in the event that, from the time beginning immediately after the Closing until the fifth anniversary of the Closing (the "Earnout Period"), the Initial Milestone Event occurs; and (ii) an additional 4,000,000 shares of the Earnout Consideration, in the event that, during the Earnout Period, the Final Milestone Event occurs. Approximately 91% of Orchestra BioMed, Inc. stockholders elected to participate in the Earnout. On April 12, 2023, the Initial Milestone Event was achieved, and each Earnout Participant was issued their Pro Rata Portion (as such term is defined in the merger agreement for the Business Combination) of 4,000,000 shares of Company Common Stock, resulting in a total of 3,999,987 shares of Company Common Stock being issued (less than 4,000,000 due to rounding).

Diluted net loss per share of Company Common Stock includes the effect, if any, from the potential exercise or conversion of securities, such as stock options, Orchestra BioMed, Inc. Warrants, Private Warrants, Officer and Director Warrants, Forfeitable Shares, Earnout Consideration, and Series A Preferred Stock, using the if-converted method, which would result in the issuance of incremental shares of Company Common Stock, unless their effect would be anti-dilutive.

The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per share for the years ended December 31, 2025 and 2024, as their effect is anti-dilutive:

	Year Ended December 31,	
	2025	2024
Stock options	7,199,571	5,696,845
Company common stock warrants	4,148,146	1,997,812
Unvested restricted stock units	2,300,651	2,094,584
Series A Preferred Stock	1,666,666	—
Forfeitable shares	500,000	500,000
Earnout consideration	4,000,000	4,000,000
Total	**19,815,034**	**14,289,241**

19. Subsequent Events

On January 9, 2026, Haemonetics Corporation, a global medical technology company focused on delivering innovative solutions designed to improve patient outcomes, announced its acquisition of Vivasure. Vivasure was a strategic investment of the Company prior to its acquisition. In connection with the closing of the transaction, the Company can receive up to approximately $10.7 million of proceeds in 2026 associated with the transaction. In January, the Company received the initial upfront payment of $4.7 million and the remainder may be received in 2026 based on the achievement of a milestone. The Company may receive additional proceeds in the future associated with revenue earnouts based on the achievement of certain milestones.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

We maintain "disclosure controls and procedures" (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), that are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2025, the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2025.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting refers to the process designed by, or under the supervision of, our principal executive officer and principal financial officer, and effected by our Board, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorization of our management and directors; and

(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisitions, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. In making the assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control - Integrated Framework (2013).

Based on our assessment, our management has concluded that, as of December 31, 2025, our internal controls over financial reporting were effective based upon those criteria.

Attestation Report of Registered Public Accounting Firm

We are a "smaller reporting company" as such term is defined under the Exchange Act. This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption for certain "smaller reporting companies." We will continue to not be required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002 as long as (a) our annual revenue is less than $100.0 million during the most recently completed fiscal year and (b) the market value of our voting and non-voting common stock held by non-affiliates is less than $700.0 million as of the last business day of the second quarter of such fiscal year.

Changes in Internal Control Over Financial Reporting.

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2025 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitation on the Effectiveness of Internal Control.

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures, or our internal controls, will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within our Company have been detected.

Item 9B. Other Information.

Rule 10b5-1 Trading Arrangements

During the quarter ended December 31, 2025, none of our directors or officers (as defined in Rule 16a-1(f) under the Exchange Act) adopted, modified or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement" (as those terms are defined in Item 408 of Regulation S-K), except as follows:

- On December 18, 2025, Darren Sherman, our President and Chief Operating Officer, adopted a Rule 10b5-1 trading arrangement for the sale of up to 180,000 shares of our common stock, subject to certain conditions. Sales under Mr. Sherman's Rule 10b5-1 trading arrangement do not commence until June 2026, and the arrangement's expiration date is May 28, 2027.

- On December 18, 2025, Andrew Taylor, our Chief Financial Officer, adopted a Rule 10b5-1 trading arrangement for the sale of up to 84,000 shares of our common stock, subject to certain conditions. Sales under Mr. Taylor's Rule 10b5-1 trading arrangement do not commence until July 2026, and the arrangement's expiration date is June 30, 2027.

Each of Messrs. Sherman and Taylor have designated a minimum target price for the sale of their shares of common stock under their respective Rule 10b5-1 trading arrangements. If our common stock is not trading at or above the respective target prices set by Mr. Sherman or Mr. Taylor, then such officer's shares will not be sold pursuant to such officer's Rule 10b5-1 trading arrangement.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The Company has adopted insider trading policies and procedures governing the purchase, sale, and/or other dispositions of the Company's securities by directors, officers and employees that are reasonably designed to promote compliance with insider trading laws, rules and regulations, and any listing standards applicable to the Company. The Amended and Restated Orchestra BioMed Holdings, Inc. Insider Trading Policy is filed as Exhibit 19.1 to this Annual Report on Form 10-K.

All other information required by this Item 10 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2025.

Item 11. Executive Compensation

The information required by this Item 11 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2025.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2025.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2025.

Item 14. Principal Independent Accountant Fees and Services

The information required by this Item 14 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2025.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements

Reference is made to the Index to Financial Statements appearing on page 149 of Item 8 of this Annual Report on Form 10-K.

(a)(2) All other schedules not listed above have been omitted because of the absence of conditions under which they are required, or because the required information is included in the consolidated financial statements or the notes thereto.

(a)(3) Exhibits

The following exhibits are filed herewith or incorporated herein by reference:

Exhibit	Description
2.1#	Agreement and Plan of Merger dated as of July 4, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc. (incorporated by reference to Annex A-1 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
2.2#	Amendment No. 1 to Agreement and Plan of Merger dated as of July 21, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc. (incorporated by reference to Annex A-2 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022)).
2.3#	Amendment No. 2 to Agreement and Plan of Merger dated as of November 21, 2022 by and among Health Sciences Acquisitions Corporation 2, HSAC Olympus Merger Sub, Inc., and Orchestra BioMed, Inc. (incorporated by reference to Annex A-3 of Amendment No. 4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
3.1	Certificate of Incorporation of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
3.2	Certificate of Designation of Series A Convertible Preferred Stock, dated November 6, 2025 (incorporated by reference to Exhibit 3.2 to the Quarterly Report on Form 10-Q filed with the SEC on November 10, 2025).
3.3	Amended and Restated Bylaws of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 3.2 to the Quarterly Report on Form 10-Q filed with the SEC on August 12, 2024).
4.1	Form of Common Stock Warrant, issued by Orchestra BioMed, Inc. in the Formation Mergers in exchange for Caliber, BackBeat and FreeHold warrants (incorporated by reference to Exhibit 4.4 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.2	Form of Amendment to Common Stock Warrant, issued by Orchestra BioMed, Inc. in the Formation Mergers in exchange for Caliber, BackBeat and FreeHold warrants (incorporated by reference to Exhibit 4.5 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.3	Form of Amended and Restated Common Stock Warrant, issued by Orchestra BioMed, Inc. to designees of Aegis Capital Corp. (incorporated by reference to Exhibit 4.6 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.4	Form of Special Advisory Common Stock Warrant, issued by Orchestra BioMed, Inc. to its strategic advisers, dated May 31, 2018 (incorporated by reference to Exhibit 4.7 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.5	Form of Amendment to Special Advisory Common Stock Warrant, issued by Orchestra BioMed, Inc. to its strategic advisers (incorporated by reference to Exhibit 4.8 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.6	Form of Common Stock Warrant, issued by Orchestra BioMed, Inc. to SLD Capital Corp., dated August 13, 2018 (incorporated by reference to Exhibit 4.9 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).

Exhibit	Description
4.7	Form of Amendment to Common Stock Warrant, issued by Orchestra BioMed, Inc. to SLD Capital Corp. (incorporated by reference to Exhibit 4.10 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.8	Investors' Rights Agreement, by and among Orchestra BioMed, Inc. and the investors listed on Schedule A thereto, dated May 31, 2018 (incorporated by reference to Exhibit 4.11 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.9	Form of Subscription Agreement for shares of Orchestra BioMed, Inc. Series B-1 Preferred Stock (incorporated by reference to Exhibit 4.12 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.10	Common Stock Warrant, issued by Orchestra BioMed, Inc. to Avenue Venture Opportunities Fund, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 4.14 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.11	Common Stock Warrant, issued by Orchestra BioMed, Inc. to Avenue Venture Opportunities Fund II, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 4.15 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.12	Form of Officer and Director Warrant issued pursuant to the Merger Agreement (incorporated by reference to Exhibit 4.16 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
4.13	Amended & Restated Warrant issued to HSAC 2 Holdings, LLC, dated January 25, 2023 (incorporated by reference to Exhibit 4.14 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
4.14	Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund, L.P., dated October 6, 2023 (incorporated by reference to Exhibit 4.14 to the Company's Form S-1 (File No. 333-274924), filed with the SEC on October 10, 2023).
4.15	Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. to Avenue Venture Opportunities Fund II, L.P., dated October 6, 2023 (incorporated by reference to Exhibit 4.15 to the Company's Form S-1 (File No. 333-274924), filed with the SEC on October 10, 2023).
4.16	Form of Warrant Agreement, dated November 6, 2024, issued in connection with the Loan and Security Agreement, dated November 6, 2024, by and among the Company and certain of its subsidiaries, the lenders named therein and Hercules Capital, Inc., as administrative agent and collateral agent for itself and the lenders (incorporated by reference to Exhibit 4.1 to the Company's Form 10-Q, filed with the SEC on November 12, 2024).
4.17	Form of Amendment No. 1 to Warrants between the Company and each of Hercules Capital, Inc., Hercules Capital IV, L.P., and Hercules SBIC V, L.P. (incorporated by reference to Exhibit 4.2 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
4.18	Form of Common Stock Warrant, issued by Orchestra BioMed Holdings, Inc. in connection with the Restated and Amended Consulting Agreement, dated January 1, 2025, by and between the Company and John Columbia, Inc. (incorporated by reference to Exhibit 4.17 to the Company's Annual Report on Form 10-K filed with the SEC on March 31, 2025).
4.19	Warrant issued to Ligand Pharmaceuticals Incorporated, dated August 4, 2025 (incorporated by reference to Exhibit 4.1 to the Quarterly Report on Form 10-Q filed with the SEC on August 12, 2025).
4.20	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed with the SEC on August 4, 2025)
4.21+	Description of Securities of Orchestra BioMed Holdings, Inc.
10.1	Second Amended and Restated Registration Rights and Lock-Up Agreement, dated November 21, 2023, by and among Orchestra BioMed Holdings, Inc., equityholders thereof and certain former stockholders of Orchestra BioMed, Inc. (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on November 28, 2023)
10.2*	Form of Indemnification Agreement of Orchestra BioMed Holdings, Inc. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).

Exhibit	Description
10.3	Amended and Restated Parent Support Agreement dated as of November 21, 2022 by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., HSAC 2 Holdings, LLC, Alice Lee, Stephanie A. Sirota, Pedro Granadillo, Stuart Peltz, Michael Brophy, and Carsten Boess (incorporated by reference to Exhibit 10.16 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.4	Orchestra Support Agreement dated as of July 4, 2022 by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc., and Covidien Group S.À.R.L. (incorporated by reference to Exhibit 10.5 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.5	Form of Earnout Election Agreement, by and among Health Sciences Acquisitions Corporation 2, Orchestra BioMed, Inc. and the securityholders thereto (incorporated by reference to Exhibit 10.7 to HSAC2's Current Report on Form 8-K filed with the SEC on July 5, 2022).
10.6*	Orchestra BioMed, Inc. 2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.19 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.7*	Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.8*	Form of Stock Option Grant Notice and Stock Option Agreement under the Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.8 to the Current Report on Form 8- K filed with the SEC on January 31, 2023).
10.9*	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the Orchestra BioMed Holdings, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.10^	Commercial Lease, by and between Caliber Therapeutics, Inc. and Union Square, L.P. for facilities at 150 and 140 Union Square Drive, New Hope, Pennsylvania, dated December 14, 2009 and amended June 22, 2010, February 1, 2011, September 18, 2012, January 15, 2015, January 20, 2017, August 8, 2017, January 29, 2019, August 30, 2019 and August 8, 2024 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 12, 2024).
10.11	Agreement of Lease, by and between Orchestra BioMed, Inc. and ESRT One Grand Central Place, L.L.C. for facilities at Room/Suite 2430, One Grand Central Place, 60 East 42nd Street, New York, New York, dated November 5, 2019 (incorporated by reference to Exhibit 10.24 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.12#	First Amendment of Lease dated as of November 22, 2022, by and between ESRT One Grand Central Place, L.L.C., and Orchestra BioMed, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 13, 2024).
10.13^	Lease Agreement, dated as of September 9, 2024, by and between Victoriana Building, LLC and Orchestra BioMed, Inc. (incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K filed with the SEC on March 31, 2025).
10.14	License Agreement, by and between MOTUS GI Holdings, Inc. and Orchestra BioMed, Inc. for facilities at Suite 310, 1301 East Broward Boulevard, Fort Lauderdale, Florida, dated January 22, 2020 (incorporated by reference to Exhibit 10.26 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.15	Amendment to License Agreement, by and between MOTUS GI Holdings, Inc. and Orchestra BioMed, Inc., dated May 1, 2022 (incorporated by reference to Exhibit 10.27 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.16^	Exclusive License and Collaboration Agreement, by and among Orchestra BioMed, Inc., BackBeat Medical, LLC, and Medtronic, Inc. dated June 30, 2022 (incorporated by reference to Exhibit 10.28 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.17^	Distribution Agreement, by and among Orchestra BioMed, Inc., Terumo Corporation and Terumo Medical Corporation, dated June 13, 2019 (incorporated by reference to Exhibit 10.29 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).

Exhibit	Description
10.18^	Letter Agreement to Distribution Agreement, by and among Orchestra Biomed, Inc., Terumo Corporation and Terumo Medical Corporation, dated June 13, 2019 (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K filed with the SEC on March 31, 2025).
10.19^	Amendment to Distribution Agreement, by and among Orchestra Biomed, Inc., Terumo Corporation and Terumo Medical Corporation, dated June 30, 2020 (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K filed with the SEC on March 31, 2025).
10.20	Loan and Security Agreement, by and among Orchestra BioMed, Inc., Avenue Venture Opportunities Fund II, L.P., and Avenue Venture Opportunities Fund II, L.P., dated June 3, 2022 (incorporated by reference to Exhibit 10.28 of HSAC2's Form S-4 (File No. 333-266660), filed with the SEC on December 12, 2022).
10.21#	Loan and Security Agreement, dated November 6, 2024, by and among the Company and certain of its subsidiaries, the lenders named therein and Hercules Capital, Inc., as administrative agent and collateral agent for itself and the lenders (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 12, 2024).
10.22*#	Employment Agreement, by and between Orchestra BioMed Holdings, Inc. and David P. Hochman, dated January 26, 2023 (incorporated by reference to Exhibit 10.19 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.23*#	Employment Agreement, by and between Orchestra BioMed Holdings, Inc. and Darren R. Sherman, dated January 26, 2023 (incorporated by reference to Exhibit 10.20 to the Current Report on Form 8-K filed with the SEC on January 31, 2023).
10.24*	Offer Letter, dated as of June 5, 2023, by and between the Company and Andrew Taylor (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on June 8, 2023).
10.25*	Bonus Letter Agreement, dated November 8, 2024, by and between the Company and Darren Sherman (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 12, 2024).
10.26	Orchestra BioMed Holdings, Inc. Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.33 to the Company's Annual Report on Form 10-K filed with the SEC on March 27, 2024).
10.27	Revenue Participation Right Purchase and Sale Agreement, by and between the Company and Ligand Pharmaceuticals Inc., dated July 31, 2025 (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
10.28	Stock Purchase Agreement, by and between the Company and Ligand Pharmaceuticals Incorporated, dated July 31, 2025 (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
10.29	Loan Agreement, by and among the Company, Orchestra BioMed, Inc, BackBeat Medical, LLC and Medtronic Inc., dated July 31, 2025 (incorporated by reference to Exhibit 10.3 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
10.30	Form of Secured Subordinated Promissory Note by and among the Company, Orchestra BioMed, Inc, BackBeat Medical, LLC and Medtronic Inc. (incorporated by reference to Exhibit 10.4 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
10.31	Stock Purchase Agreement, by and between the Company and Covidien Group S.à.r.l., dated July 31, 2025 (incorporated by reference to Exhibit 10.5 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).
10.32	Amendment No. 1 to Stock Purchase Agreement, by and between the Company and Covidien Group S.à.r.l., dated August 1, 2025 (incorporated by reference to Exhibit 10.6 to the Quarterly Report on Form 10-Q filed with the SEC on August 12, 2025).
10.33	Second Amendment to Loan and Security Agreement, by and among the Company and certain of its subsidiaries, the lenders named therein and Hercules Capital, Inc., dated July 31, 2025 (incorporated by reference to Exhibit 10.6 to the Current Report on Form 8-K filed with the SEC on July 31, 2025).

Exhibit	Description
10.34	Registration Rights Agreement, dated August 4, 2025, by and among the Company, Ligand Pharmaceuticals Incorporated and Covidien Group S.à.r.l. (incorporated by reference to Exhibit 10.8 to the Quarterly Report on Form 10-Q filed with the SEC on August 12, 2025).
10.35	Amendment No. 1 to Exclusive License and Collaboration Agreement, dated as of August 1, 2025, by and among the Company, BackBeat Medical, LLC and Medtronic, Inc. (incorporated by reference to Exhibit 10.9 to the Quarterly Report on Form 10-Q filed with the SEC on August 12, 2025).
10.36	Termination and ROFR Agreement, by and between the Orchestra BioMed, Inc., Terumo Corporation and Terumo Medical Corporation, dated October 24, 2025 (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed with the SEC on October 28, 2025).
10.37	Stock Purchase Agreement, by and between the Company and Terumo Medical Corporation, dated October 24, 2025 (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed with the SEC on October 28, 2025).
10.38	Lockup Agreement, by and among the Company, Terumo Corporation and Terumo Medical Corporation, dated October 24, 2025 (incorporated by reference to Exhibit 10.3 to the Current Report on Form 8-K filed with the SEC on October 28, 2025).
10.39	Orchestra BioMed Holdings, Inc. 2025 New Hire Inducement Plan (incorporated by reference to Exhibit 10.13 to the Quarterly Report on Form 10-Q filed with the SEC on November 10, 2025).
10.40	Form of Stock Option Grant Notice and Stock Option Agreement for the Orchestra BioMed Holdings, Inc. 2025 New Hire Inducement Plan (incorporated by reference to Exhibit 10.14 to the Quarterly Report on Form 10-Q filed with the SEC on November 10, 2025).
10.41	Form of Restricted Stock Unit Grant Notice and Award Agreement for the Orchestra BioMed Holdings, Inc. 2025 New Hire Inducement Plan (incorporated by reference to Exhibit 10.15 to the Quarterly Report on Form 10-Q filed with the SEC on November 10, 2025).
14.1	Orchestra BioMed Holdings, Inc. Code of Business Conduct and Ethics (Incorporated by reference to Exhibit 14.1 to the Company's Annual Report on Form 10-K filed with the SEC on March 27, 2024).
19.1	Amended and Restated Orchestra BioMed Holdings, Inc. Insider Trading Policy (Incorporated by reference to Exhibit 19.1 to the Company's Annual Report on Form 10-K filed with the SEC on March 27, 2024).
21.1+	List of Subsidiaries of Orchestra BioMed Holdings, Inc.
23.1+	Consent of Ernst & Young LLP, independent registered public accounting firm of Orchestra BioMed Holdings, Inc.
24.1+	Power of Attorney (included on the signature page to this Annual Report on Form 10-K).
31.1+	Certification of Chief Executive Officer, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2+	Certification of Chief Financial Officer, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+†	Certification of Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2+†	Certification of Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Orchestra BioMed Holdings, Inc. 2023 Executive Incentive Compensation Recoupment Policy (Incorporated by reference to Exhibit 97.1 to the Company's Annual Report on Form 10-K filed with the SEC on March 27, 2024).
101.INS+	Inline XBRL Instance Document.
101.SCH+	Inline XBRL Taxonomy Extension Schema Document.
101.CAL+	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF+	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB+	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE+	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104+	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

+ Filed herewith.

Certain of the exhibits and schedules to this Exhibit have been omitted in accordance with Regulation S-K Item 601. The Registrant agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon its request.

* Indicates a management contract or compensatory plan.

^ Certain identified information has been omitted pursuant to Item 601(b)(10) of Regulation S-K because such information is both (i) not material and (ii) information that the Registrant treats as private or confidential. The Registrant hereby undertakes to furnish supplemental copies of the unredacted exhibit upon request by the SEC.

† This exhibit shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section. Such exhibit shall not be deemed incorporated into any filing under the Securities Act or the Exchange Act.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ORCHESTRA BIOMED HOLDINGS, INC.

Date: March 12, 2026

By: /s/ David P. Hochman
Name: David P. Hochman
Title: Chief Executive Officer
(*Principal Executive Officer*)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David P. Hochman and Andrew L. Taylor, and each of them, as his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ David P. Hochman David P. Hochman	Chief Executive Officer, Chairperson and Director (*Principal Executive Officer*)	March 12, 2026
/s/ Andrew L. Taylor Andrew L. Taylor	Chief Financial Officer (*Principal Financial Officer*)	March 12, 2026
/s/ Joshua Aiello Joshua Aiello	Corporate Controller (*Principal Accounting Officer*)	March 12, 2026
/s/ Jason Aryeh Jason Aryeh	Director	March 12, 2026
/s/ Chris Cleary Chris Cleary	Director	March 12, 2026
/s/ Pamela A. Connealy Pamela A. Connealy	Director	March 12, 2026
/s/ Eric S. Fain, M.D. Eric S. Fain, M.D.	Director	March 12, 2026
/s/ John Mack John Mack	Director	March 12, 2026
/s/ David Pacitti David Pacitti	Director	March 12, 2026
/s/ Darren R. Sherman Darren R. Sherman	President, Chief Operating Officer and Director	March 12, 2026