Orchestra BioMed

Corporate Overview

June 2026

Nasdaq: OBIO

Forward-Looking Statements

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

Certain statements included in this document that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements relating to the potential safety and efficacy of our product candidates, the enrollment and timing of our pivotal trials and reporting of top-line results, the timing of regulatory submissions, expected market sizes for our product candidates, the ability of our partnerships to accelerate clinical development and the benefits of Breakthrough Device Designation. These statements are based on various assumptions, whether or not identified in this document, and on the current expectations of the Company's management and are not predictions of actual performance. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as and must not be relied on as a guarantee, an assurance, a prediction, or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and may differ from assumptions. Many actual events and circumstances are beyond the control of the Company. These forward-looking statements are subject to a number of risks and uncertainties, including changes in domestic and foreign business, market, financial, political, and legal conditions; risks related to regulatory approval of the Company's product candidates; the timing of, and the Company's ability to achieve expected regulatory and business milestones; the impact of competitive products and product candidates; and the risk factors discussed under the heading "Item 1A. Risk Factors" in the Company's annual report on Form 10-K filed with the U.S. Securities and Exchange Commission on March 12, 2026 as updated by any risk factors disclosed under the heading "Item 1A. Risk Factors" in Part II of the Company's subsequently filed quarterly reports on Form 10-Q.

The Company operates in a very competitive and rapidly changing environment. New risks emerge from time to time. Given these risks and uncertainties, the Company cautions against placing undue reliance on these forward-looking statements, which only speak as of the date of this presentation. The Company does not plan and undertakes no obligation to update any of the forward-looking statements made herein, except as required by law.

The Orchestra BioMed Opportunity

Leveraging Partnerships to Accelerate Innovation for Patients & Yield Exceptional Profitability

Two Pivotal Trial-Stage Flagship Technologies

Address significant **unmet needs across large, established** global cardiovascular markets

Capital-Efficient Business Model

Aims to generate **substantial royalty-based revenue** from partner-driven commercialization

Major Primary Data Readout Targeted for Q2 2027

Funding in place is expected to enable operations through the **BACKBEAT Trial data readout** and **Virtue Trial enrollment**

Two Pivotal Trial-Stage Flagship Technologies

AVIM Therapy

Atrioventricular Interval Modulation (AVIM) Therapy

- First-of-its-kind **cardiac pacing-based therapy** for hypertension and hypertensive heart disease
- **Pivotal Trial** targeting enrollment completion by end of Q3 2026 and data presentation in Q2 2027
- Two **FDA Breakthrough Device Designations***

>$17B

Annual global market opportunity

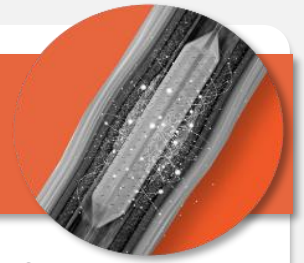
Strategic Collaboration

Medtronic

Double-digit revenue share

Virtue SAB

Virtue Sirolimus AngioInfusion™ Balloon (SAB)



- Highly differentiated **drug delivery system** for treatment of artery disease
- **Pivotal Trial** initiated in Q4 2025 and targeting enrollment completion in 2027
- Three **FDA Breakthrough Device Designations**

>$10B

Annual global market opportunity

Strategic Rights Agreement

TERUMO

Right of First Refusal (Coronary)

*The U.S. FDA granted Breakthrough Device Designation for an implantable system (i.e., a pacemaker) to deliver AVIM Therapy using conduction system pacing to reduce blood pressure in patients with increased ten-year atherosclerotic cardiovascular disease risk, preserved left ventricular systolic function, and uncontrolled hypertension, despite the use of anti-hypertensive medications or in patients who may have intolerance to anti-hypertensive medications.

FDA granted a second BDD for AVIM Therapy specific to patients with uncontrolled hypertension despite the use of anti-hypertensive medications, and an indication for a pacemaker.

Orchestra BioMed™

Expert Leadership, Proven Impact

Our leadership team is **highly experienced**, has a **successful track record** of bringing high-impact medical technologies to market, and includes individuals who have **worked together for years**

300+
Combined years in the industry experience

25+
Average years of experience, bringing deep expertise to every challenge

100+
Successful product approvals, delivering innovation globally

600+
Authored patents shaping the future of healthcare

Independent Board Members

Jason Aryeh
LIGAND · ANEBULO

Pamela Connealy
PYXIS ONCOLOGY · IMMUNOVANT · kiva · salesforce · Genentech · Bill & Melinda Gates foundation

Chris Cleary
Medtronic · GE Capital

Eric S. Fain, M.D.
Procyrion · Abbott · St. Jude Medical

David Pacitti
AVANOS · SIEMENS Healthineers · Abbott

John Mack
Medtronic · D.

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AVIM Therapy

First-of-its-kind, proprietary **cardiac pacing-based therapy for hypertension and hypertensive heart disease**

Designed to drive **immediate, substantial, and sustained** blood pressure reductions delivered via a pacemaker

Supported by **robust clinical and mechanistic data** and nearing completion of **global pivotal randomized trial**

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AVIM Therapy Addresses a Large & Clearly Defined Global Opportunity

INITIAL MARKET

HTN + Pacemaker

1M addressable patients per year

~70% of pacemaker patients

>$2 Billion

EXPANSION MARKET

Hypertensive Heart Disease

3.7M addressable patients per year

~0.3% of HTN patients

>$15 Billion

Initial market leverages same **patients**, **implants**, and **physicians**; Existing **reimbursement structure** with potential upside

Blood pressure reduction in older, higher-risk patients **lowers risk of MI, stroke and heart failure**

Potential benefit in Heart Failure with preserved Ejection Fraction (HFpEF) patients with HTN

*Total addressable market based on company estimates based on published sources, including National Inpatient Survey (NIS) and National Health and Nutrition Examination Survey (NHANES); *Definition:* Hypertension (HTN)

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AVIM Therapy Strategic Collaboration with Medtronic

Orchestra BioMed™

- **Developed AVIM Therapy from concept stage**
- Owns all related intellectual property: **120 issued global patents related to hypertension**
- Conducted all prior development and the MODERATO I & II clinical studies
- Sponsor for the BACKBEAT Global Pivotal Study

$500 - $1,600 revenue share per AVIM-enabled device assuming existing reimbursement structures[1]

Medtronic

- Global market leader in cardiac pacing therapy: **>$2B in annual revenues**
- Exclusive global commercial rights for initial market (HTN + Pacemaker), including leadless pacemakers
- Responsible for regulatory approvals, marketing, sales, support and manufacturing*
- **Right of first negotiation** for expansion market (HTN + Increased CV Risk)

$81.6M invested in Orchestra BioMed

[1] Amount is based on higher of (1) a fixed dollar amount per device (amount varies materially on a country-by-county basis) or (2) a percentage of sales

* Pending successful BACKBEAT Trial readout

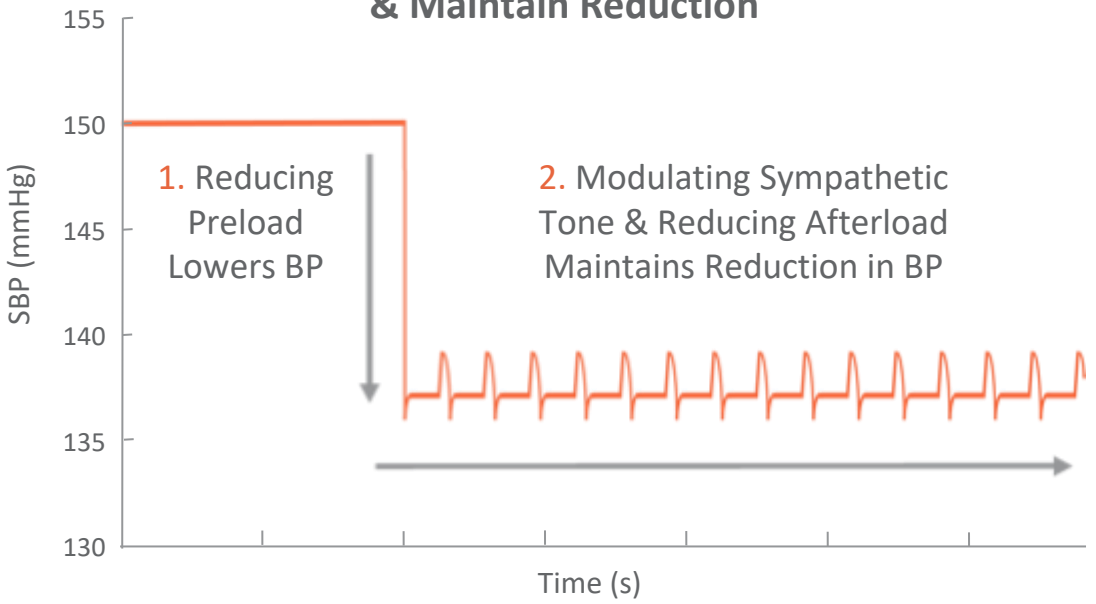
AVIM Therapy is a Novel Investigational Treatment to Reduce Blood Pressure

Designed to Have an Immediate, Substantial, & Sustained Effect[1,2,3]

Atrioventricular Interval Modulation (AVIM) Therapy

- Delivered via a dual-chamber pacemaker
- **No additional surgical procedure** and compatible with **both RV and conduction system pacing**
- Programmable, **adjustable,** and **not dependent on patient adherence**

Designed to Substantially Lower Blood Pressure (BP) & Maintain Reduction



Short AV intervals: reduce cardiac preload, **immediately lowering BP**

Intermittent longer AV intervals: modulate ANS response (baroreceptor reflex) & reduce afterload (TPR), **sustaining BP reduction**

[1]Kuck, Hemodynamic Effects of AVIM Therapy, THT'24. [2]Kalarus et al., *Journal of the American Heart Association*. 2021;10:e020492. [3]Burkhoff, MODERATO II Study 2-Year Results, TCT 2021. ***Definitions:*** RV (Right Ventricular), AV (Atrioventricular), ANS (Autonomic Nervous System), BP (Blood pressure), TPR (Total Peripheral Resistance).

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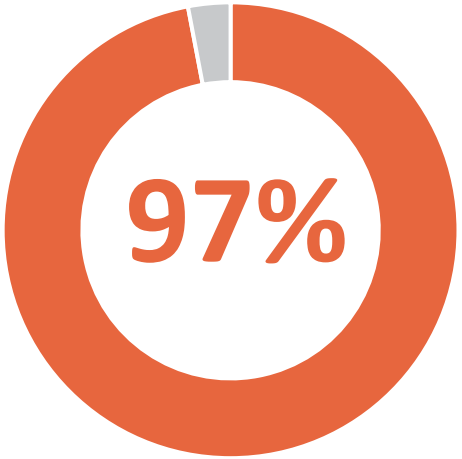
MODERATO II: Immediate Effect at Set-up

AVIM Therapy Demonstrated the Potential to Immediately, Significantly, and Substantially Reduced oSBP with a High Response Rate

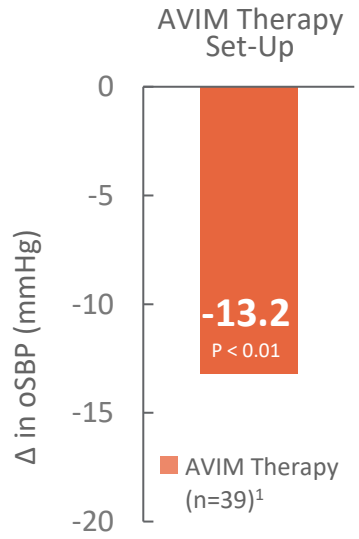
- Randomized, prospective, multi-center, double-blind, pilot study
- Pacemaker patients with hypertension despite medical therapy (≥ 1 anti-hypertensive medication)
- Screening: oSBP ≥ 140 mmHg
- Eligibility: Daytime aSBP ≥ 125 mmHg
- LVEF ≥ 50%

Immediate Response Rate at AVIM Therapy Set-Up



≥ 5 mmHg Reduction

Reduction in oSBP



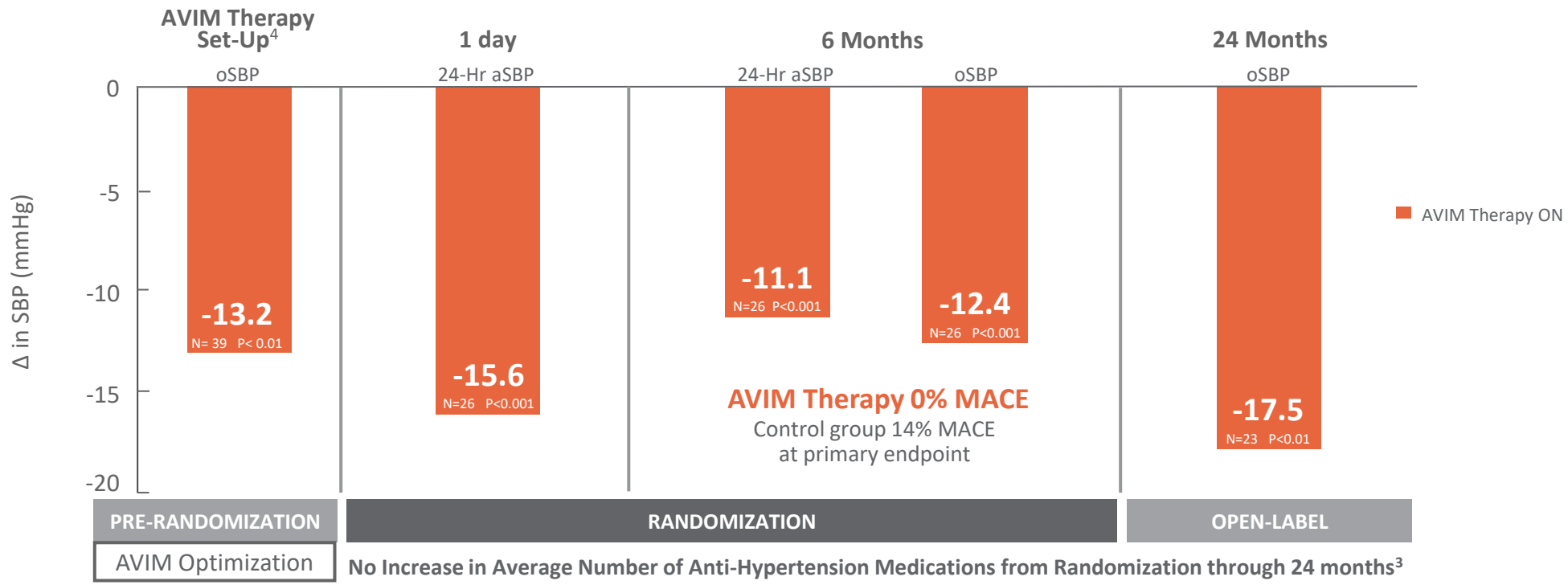
PRE-RANDOMIZATION

AVIM Optimization

[1]Includes AVIM therapy and control patients at pre-randomization and excludes the first 8 patients of the 47 in MODERATO II using different set-up methodology compared to BACKBEAT Global Pivotal Trial methodology. ***Definitions***: oSBP (office Systolic Blood Pressure), aSBP (ambulatory Systolic Blood pressure).

MODERATO II: Clinically Meaningful Results

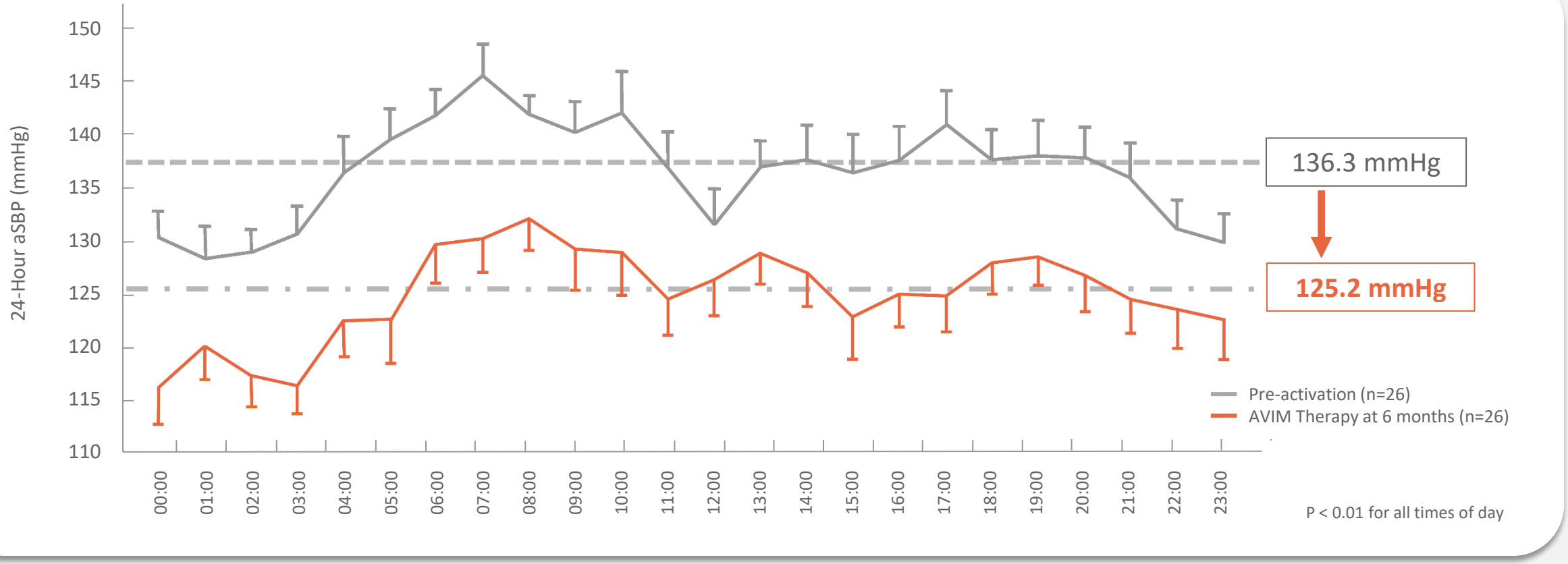
AVIM Therapy Significantly Reduced Systolic Blood Pressure Compared to Control (P< 0.02) with No Medication Changes and Low MACE[1,2]



[1]Kalarus Z, et al., *J Am Heart Assoc*. 2021;10:e020492. [2]Burkhoff, MODERATO II Study 2-Year Results, TCT 2021. [3]Fischer, AVIM therapy for management of hypertension, HRX 2025. [4]Includes AVIM therapy and control patients at pre-randomization using BACKBEAT Trial set-up methodology. ***Definitions:*** MACE (Major Adverse Cardiac Events), aSBP (ambulatory Systolic Blood Pressure), oSBP (office Systolic Blood Pressure), Hr (Hour).

MODERATO II: Significantly Reduced Ambulatory Blood Pressure

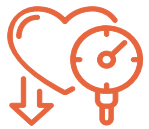
Significant Reduction in 24-Hour aSBP at 6 Months While Preserving Normal BP Pattern Throughout the Day[1]



[1]Burkhoff, MODERATO II Study 2-Year Results, TCT 2021. ***Definition:*** BP (Blood Pressure), aSBP (Ambulatory Systolic Blood Pressure).

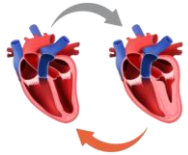
MODERATO II: Evidence of Reduced Pulse Pressure, Improved Diastolic Dysfunction, and Reverse Remodeling

Clinical data demonstrate AVIM Therapy can potentially reduce pulse pressure, improve diastolic dysfunction and induce reverse remodeling in older, higher-risk patients



- In the challenging-to-treat Isolated Systolic Hypertension patients (ISH), AVIM Therapy significantly reduced pulse pressure, **an independent risk factor** for heart failure and stroke [1,2]

- In a retrospective, blinded, independent analysis, AVIM Therapy demonstrated **improved myocardial relaxation & diastolic compliance** in patients with Diastolic Dysfunction[3]



- In a published, noninvasive pressure volume loop study, AVIM Therapy **induced positive reverse remodeling**[4]

[1]Burkhoff MODERATO II Study 2-Year Results TCT 2021. [2]Vaccarino V, et al. *Am J Cardiol*. 2001. [3]Fudim M et al. *JACC: Advances*. Vol. 4, No. 7, July 2025:101896. [4]Chovanec M, et al. *JACC Clin Electrophysiol*. 2025;11:2493-2504.

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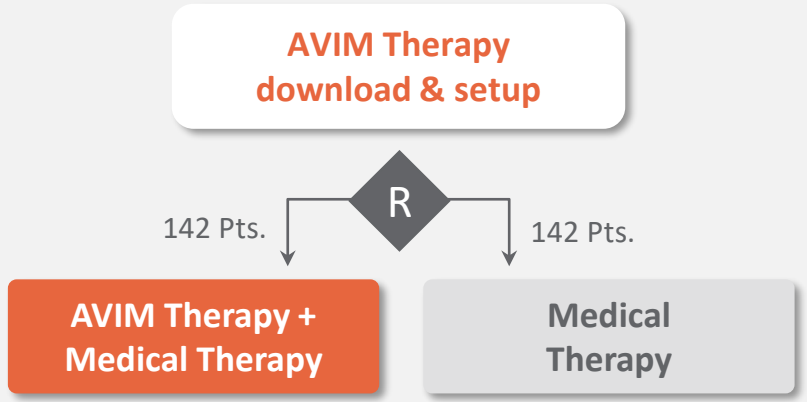
The BACKBEAT Study – Global Pivotal Hypertension Trial

Targeting completion of enrollment by end of Q3 2026 & submission of data for late-breaker in Q2 2027*

BACKBEAT
GLOBAL PIVOTAL STUDY

- Randomized, prospective, multi-center, double-blind, controlled trial
- Up to 316 patients (284 evaluable) across 130 sites in U.S., EU & APAC
- Actively enrolling trial participants

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



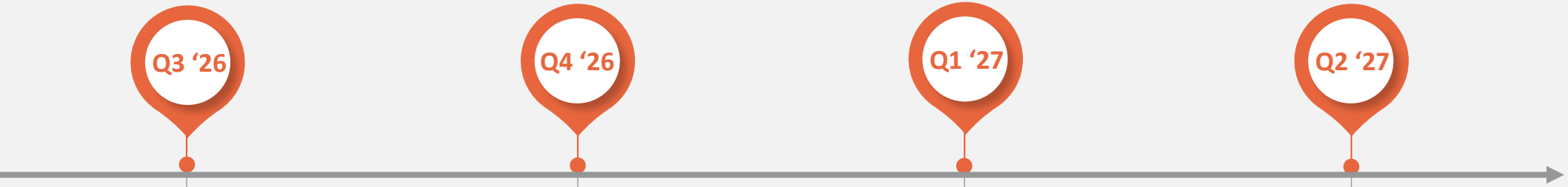
Primary Efficacy Endpoint
Between group difference in the change in mean 24-hour aSBP at 3-months

Primary Safety Endpoint
Freedom from unanticipated serious adverse device events at 3 months

Secondary Endpoints
Efficacy and safety endpoints after 12-month follow-up

*assuming primary endpoints are met

BACKBEAT Trial Milestones



Target Enrollment Completion by End of Q3

Complete Primary Endpoint Visits by End of Q4

Data Analysis & Late-Breaking Presentation Announcement

Primary Endpoint Data Late-Breaking Presentation*

FDA Marketing Application

Medtronic

*assuming primary endpoints are met and data presentation is accepted for presentation

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Virtue® SAB

First-of-its-kind drug delivery system featuring proprietary submicron **extended-release SirolimusEFR™ and non-coated, microporous AngioInfusion balloon**

Designed to provide **protected delivery of large liquid dose of sirolimus**, enabling rapid uptake and deep vessel wall penetration while extending release of therapeutic levels through the healing period

Supported by **best-in-class pilot clinical data** and **robust preclinical pharmacokinetic data**

Virtue SAB Offers Key Potential Advantages In Large, Established Global Market Opportunity

Coronary

~3.7M addressable patients per year

>$7.5 Billion

Peripheral

~1.25M addressable patients per year

>$2.5 Billion

Treatment paradigm shifting from drug-eluting stents (DESs) to drug coated balloons (DCBs)

Boston Scientific AGENT™ is currently only approved coronary DCB in U.S.

Enhanced reimbursement supports highly attractive U.S. commercial opportunity

*Total addressable market based on company estimates; Definitions: Coronary Artery Disease (CAD), Peripheral Artery Disease (PAD); Drug-eluting balloon (DEB), Drug-coated balloon (DCB), Paclitaxel-coated balloon (PCB)

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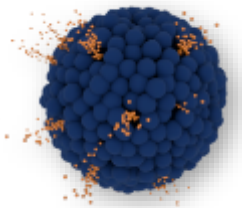
Opportunity Drivers for Virtue SAB

A Novel Solution is Required to Realize Advantages of Sirolimus

- **Superiority of sirolimus safety and efficacy over paclitaxel demonstrated** in large meta-analysis of 76 drug-eluting stent studies including 26 RCTs[1]
- **Sirolimus requires extended release through the critical healing period** to achieve full benefits (~30 days of >1ng/mg tissue concentration)
- **Paclitaxel** became "drug of choice" for coated balloons because it is **easier, not better** (fast tissue absorption and long tissue retention)
- **Coatings have challenges**, such as limited dosing, risk of emboli from large particulates, and drug loss in transit

Protected Delivery of Extended Release Sirolimus



SirolimusEFR™

+

Microporous AngioInfusion™ Balloon

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

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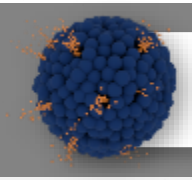
Virtue® SAB – Optimal Drug, Dose and Delivery

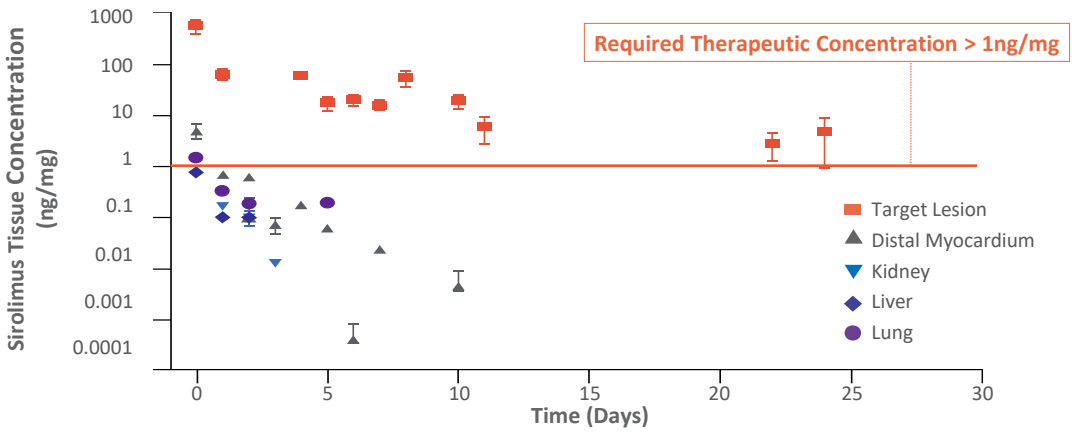


SirolimusEFR™

Protected Delivery of Extended Release Sirolimus

Microporous AngioInfusion™ Balloon

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

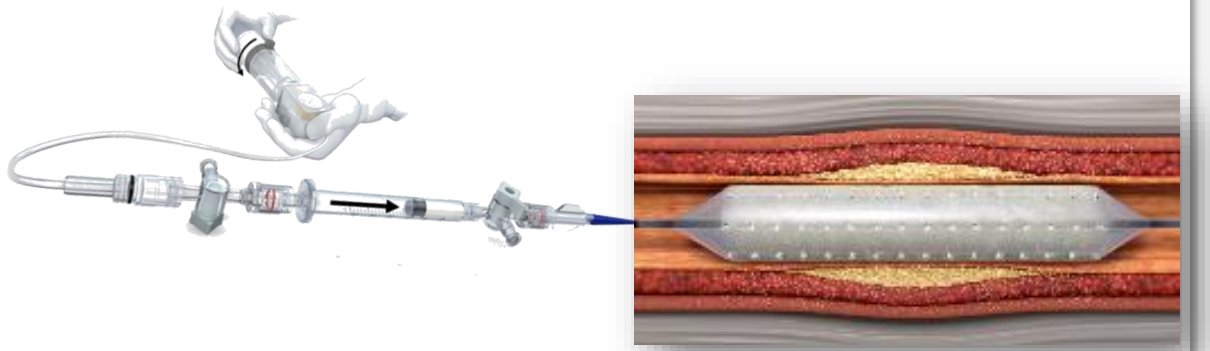


N = 753
porcine coronary artery segments

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

Large Liquid Dose Loaded and Protected in Dose Unit Delivered Through the Micropores During Inflation

NO coating = NO drug loss in transit, NO rush and NO large particulate



[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

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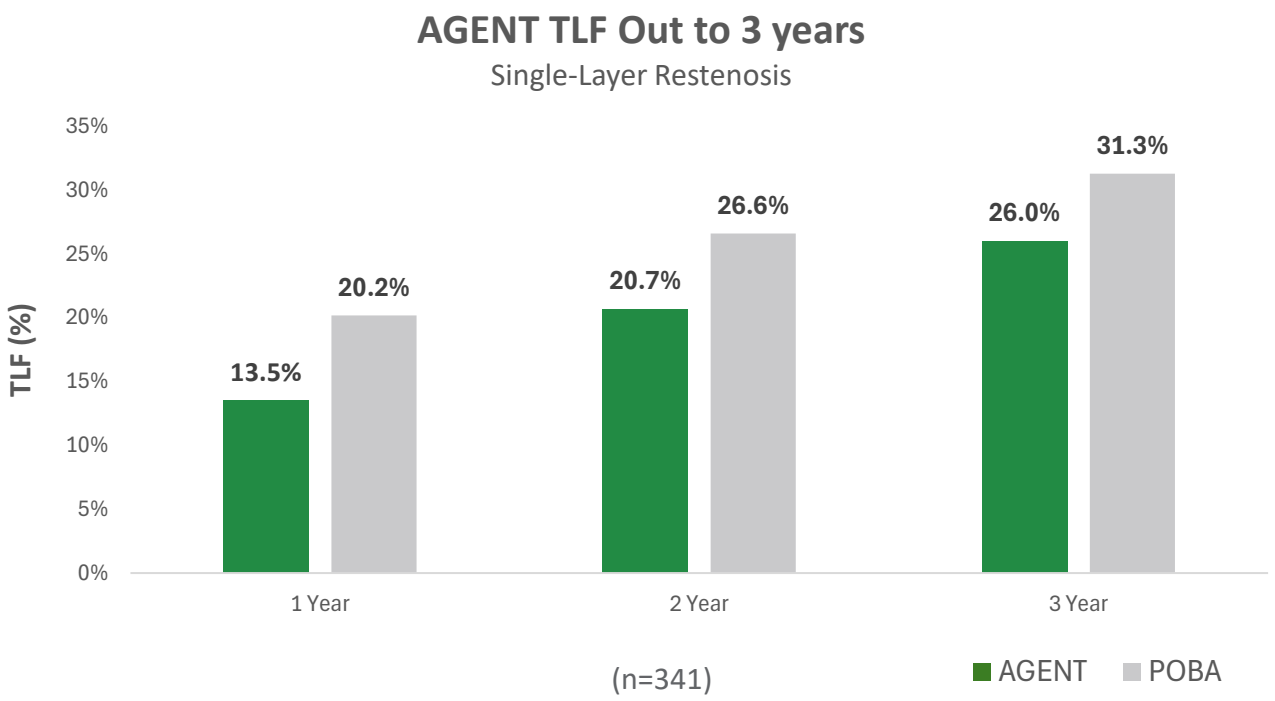
AGENT IDE Trial Results Show Clear Opportunity for Virtue SAB

Boston Scientific's Agent DCB demonstrated a reduction in TLF versus POBA in patients with single-layer restenosis in randomized IDE Trial[1,2]



AGENT 13.5% Target Lesion Failure (TLF) at 1 year

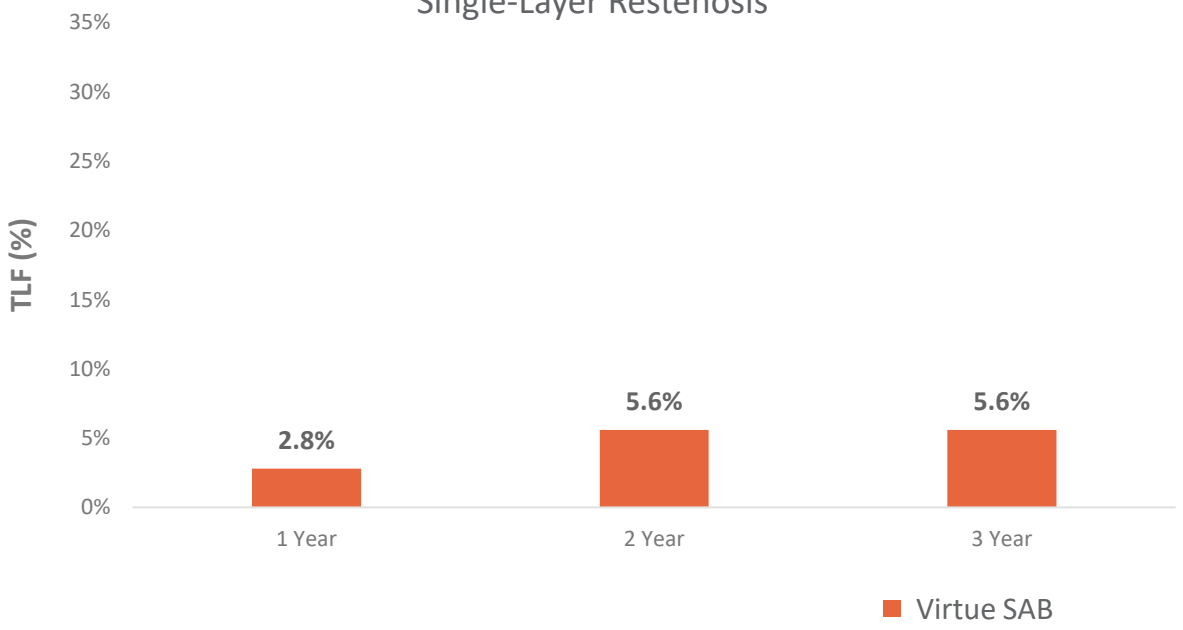
AGENT 93% relative increase in TLF from 1 to 3 years

No angiographic follow-up in IDE AGENT LLL = 0.397mm at 6 months[3]

[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:*** Drug-Coated Balloon (DCB), Plain old balloon angioplasty (POBA), late lumen loss (LLL)

Compelling SABRE Trial Results in Coronary ISR Patients

Virtue® SAB demonstrated encouraging safety and efficacy results in patients with coronary in-stent restenosis (ISR) in prospective, multi-center SABRE Trial[1,2,3,4]



Low 2.8% Target Lesion Failure (TLF) at 1 year

0% Increase Target Lesion Failure (TLF) from 2-3 years

Low 0.12mm Late Lumen Loss (LLL) at 6-months

[1]Verheye et al. JACC Cardiovasc Interv 2017 Oct 23;10(20):2029-2037. DOI: 10.1016/j.jcin.2017.06.021. [2] Revised per protocol analysis set meets the criteria of the proposed In-Stent Restenosis IDE study population. [3]Granada 3-Year Clinical Results TCT 2018. [4] Cause of death unknown - reported as multiple organ failure non cardiac and non-neurological. Adjudicated as non-device and non-procedure related ***Definitions:*** Target lesion failure (TLF), late lumen loss (LLL), target lesion revascularization (TLR).

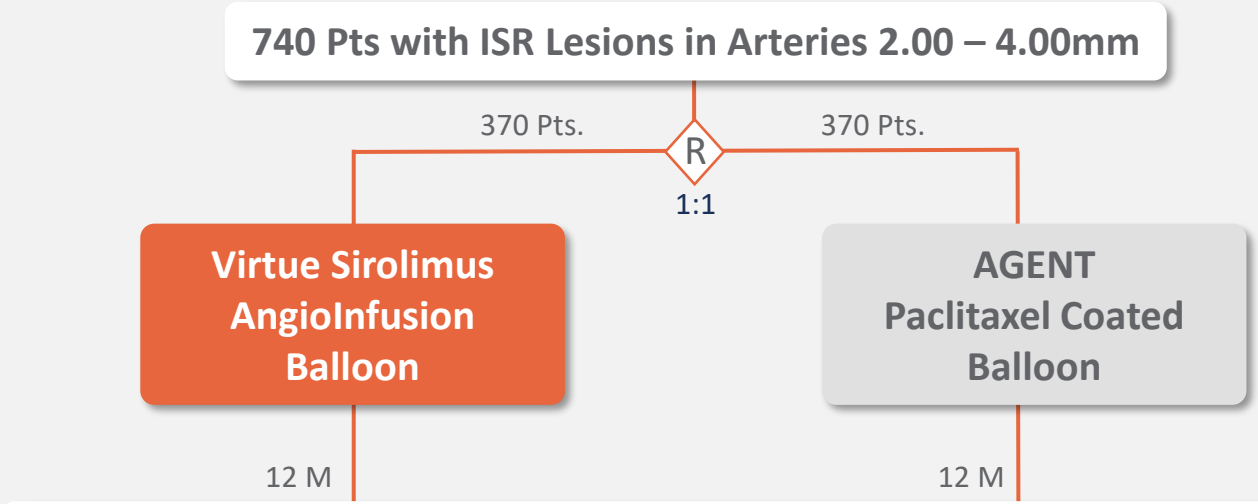
The Virtue Trial – Pivotal Coronary ISR Trial

Randomizing Virtue SAB to Commercially Available AGENT Paclitaxel-Coated Balloon

Designed to Secure Regulatory Approval & Showcase Differentiation of Virtue SAB

Virtue Trial

- FDA IDE approved
- 1:1 RCT vs AGENT
- N=740
- Primary endpoint 12-Month TLF
- Actively enrolling trial participants



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

- Primary analysis non-inferiority comparison
- Additional superiority test performed upon confirming non-inferiority

Terumo ROFR Agreement Highlights Strategic Interest & Optionality

- **Developed Virtue SAB** (SirolimusEFR, AngioInfusion balloon) **from concept stage;** owns all related IP
- Conducted all prior development work including SABRE study in coronary ISR
- Sponsoring the Virtue Trial, US pivotal coronary ISR study
- **Retains all development and distribution rights** in all indications
- Free to **engage actively with all strategic parties** and solicit proposals

- Global leader in interventional cardiology accessory devices: **>$2.4B in annual revenues[1]**
- Purchased ROFR for Virtue SAB with respect to the global coronary market
  - Has 30 days to exercise ROFR following notice of a third-party proposal acceptable to Orchestra
  - Expires 90 days after disclosure of Virtue Trial primary endpoint data
- **$65M in total payments to and investments in Orchestra**
  - $10M in consideration of ROFR, plus $20M purchase of non-voting preferred with minimum $12/share conversion after Virtue Trial results announced
  - Initially paid $30M for prior Virtue SAB rights agreement plus $5M equity investment

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

Orchestra BioMed's High-Impact Pipeline*

Two Pivotal Trial Stage Programs with Significant Future Expansion Opportunities

Target Disease	Program	Target Population	Preclinical	Clinical Feasibility	Clinical Pivotal
Hypertensive Heart Disease ***$17 Billion** Annual Global Opportunity*	**Atrioventricular Interval Modulation (AVIM) Therapy**	**Hypertension (HTN) & Pacemaker**	**BACKBEAT Global Pivotal Study Enrolling & FDA Breakthrough**		
		Hypertensive Heart Disease	**FDA Breakthrough**		
AVIM/Cardiac Neuromodulation Therapy may have additional clinical application in advanced heart failure.					
Atherosclerotic Artery Disease ***$10 Billion** Annual Global Opportunity*	**Virtue® Sirolimus AngioInfusion™ Balloon (SAB)**	**Coronary In-Stent Restenosis (ISR)**	**IDE Approved & FDA Breakthrough**		
		Coronary Small Vessel (SV)	**FDA Breakthrough**		
		Below-the-Knee (BTK)	**FDA Breakthrough**		
		Other Coronary & Peripheral Indications			
SirolimusEFR™ may have potential clinical application in a variety of non-vascular indications.					

*For more detailed information relating to our pipeline, please see the disclosure under "Item 1. Business" in our Form 10-K for the year ended December 31, 2025 filed with the SEC on March 12, 2026.

The Orchestra BioMed Opportunity

Leveraging Partnerships to Accelerate Innovation for Patients & Yield Exceptional Profitability

Two Pivotal Trial-Stage Flagship Technologies

Address significant **unmet needs across large, established** global cardiovascular markets

Capital-Efficient Business Model

Aims to generate **substantial royalty-based revenue** from partner-driven commercialization

Major Primary Data Readout Targeted for Q2 2027

Funding in place is expected to enable operations through the **BACKBEAT Trial data readout** and **Virtue Trial enrollment**

Bringing Medical Innovations to Life Through Partnerships

Orchestra BioMed