Orchestra BioMed

Corporate Overview

May 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.

Orchestra BioMed

Orchestra BioMed

Leveraging Partnerships to Bring Innovation to Patients & Yield Exceptional Profitability

Partnership-Driven Commercialization with Substantial Royalty-Based Revenue Model

Addressing Major Cardiovascular Indications in Large, Established Global Markets with Unmet Clinical Need

Funded Through Key Upcoming Milestones for AVIM Therapy and Virtue SAB Programs

BACKBEAT Trial
Targeting completion of enrollment by end of Q3 2026 & late-breaking data presentation in Q2 2027*

Virtue Trial
Enrollment ongoing & targeting completion in 2027

*assuming primary endpoints are met

Two Pivotal Trial-Stage Flagship Technologies

Targeting Major Global Unmet Needs in Cardiovascular Disease

AVIM Therapy

- **Cardiac pacing treatment** for hypertension and hypertensive heart disease
- Enrolling **BACKBEAT Global Pivotal Trial**
- Two **FDA Breakthrough Device Designations***

>$17B

Annual global market opportunity

Strategic Collaboration

Medtronic

Virtue SAB

- **Sirolimus AngioInfusion™ Balloon** for treatment of coronary and peripheral artery disease
- Enrolling **Virtue U.S. Pivotal Trial**
- Three **FDA Breakthrough Device Designations**

>$10B

Annual global market opportunity

Strategic Rights Agreement

TERUMO

*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.

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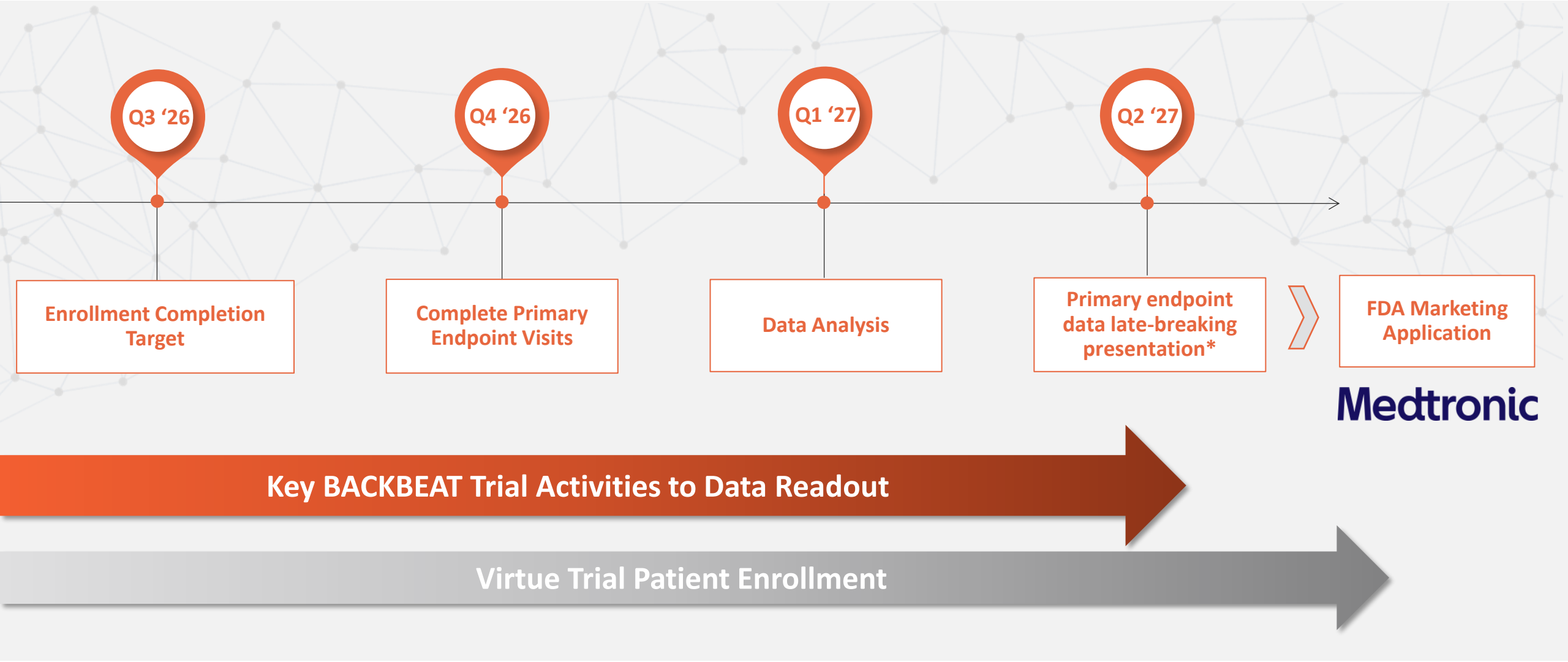
Next Four Quarters – Potential Major Milestones



*assuming primary endpoints are met

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

- Atrioventricular Interval Modulation (AVIM) Therapy

A **purpose-built solution** for uncontrolled hypertension with increased cardiovascular risk

Designed to drive **immediate, substantial, and sustained** blood pressure reduction

Supported by **robust clinical and mechanistic data**

AVIM Therapy Addresses a Large & Clearly Targeted Global Opportunity*

While **hypertension is the leading global risk factor for death**, affecting 1.2B patients worldwide, older, higher-risk patients face **hypertensive heart disease**, which directly drives increased risk of MI, stroke and heart failure.

HTN & Pacemaker

1M addressable patients per year

~70% of pacemaker patients[1]

>$2 Billion

HTN with Increased CV Risk / HFpEF

3.7M addressable patients per year

~0.3% of HTN patients

>$15 Billion

FDA Breakthrough Designations for beachhead market and beyond

Same **patients**, device **implant**, and treating **physicians**

Existing **reimbursement structure**

Uncontrolled HTN in older, higher-risk patients **drives MI, stroke and heart failure**

Potential benefit in HFpEF

*Total addressable market based on company estimates

[1]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

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- **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 pacemaker-indicated HTN patients; **recent expansion** for future leadless pacemakers
- Responsible for regulatory approvals, marketing, sales, support and manufacturing*
- **Right of first negotiation** to expand global rights for the treatment of **non-pacemaker patients with HTN**

$61.6M equity investment plus $20 million in strategic capital

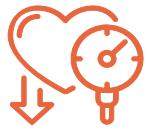
[1] Amount is based on higher of (1) a fixed dollar amount per device (amount varies materially on a country-by-county basis) or (2) a percentage of sales

* Pending successful BACKBEAT Trial readout

AVIM Therapy is a Novel Investigational Treatment to Reduce Blood Pressure

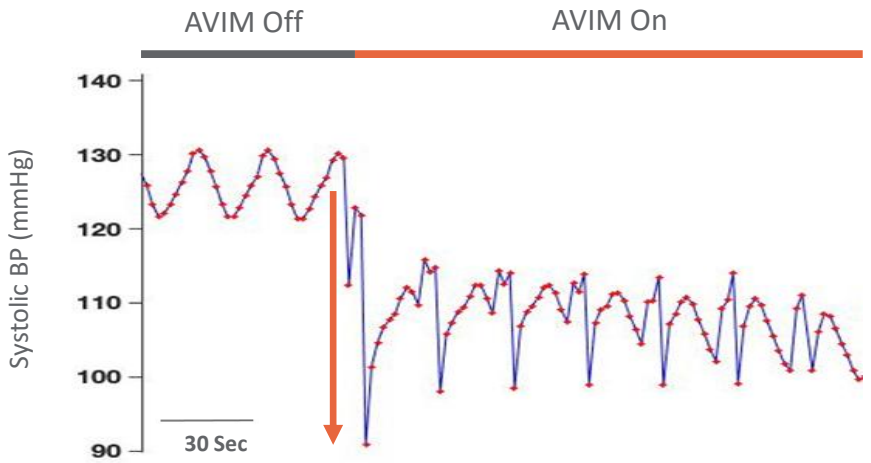
Designed to Have an Immediate, Substantial, & Sustained Effect[1,2,3]

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**

Novel & Potent Mechanism[2]



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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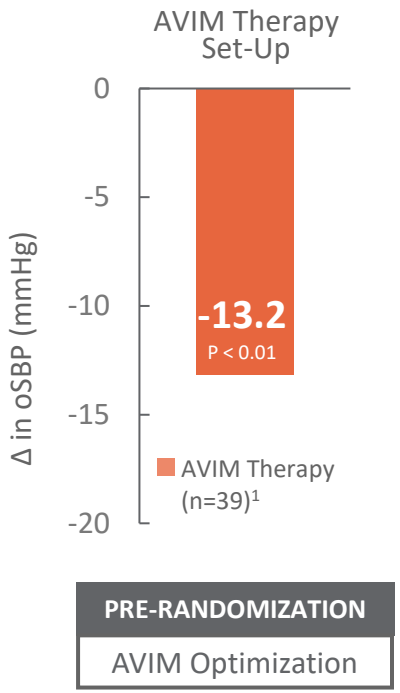
MODERATO II: Immediate Effect at Set-up

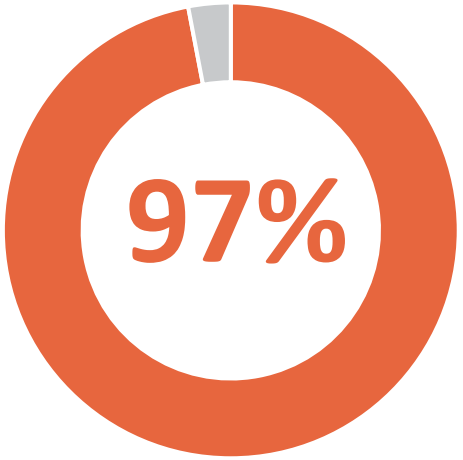
AVIM Therapy Demonstrated the Potential to Immediately, Significantly, and Substantially Reduced oSBP with a High Response Rate

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

Reduction in oSBP



Immediate Response Rate at AVIM Therapy Set-Up



≥ 5 mmHg Reduction

[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).

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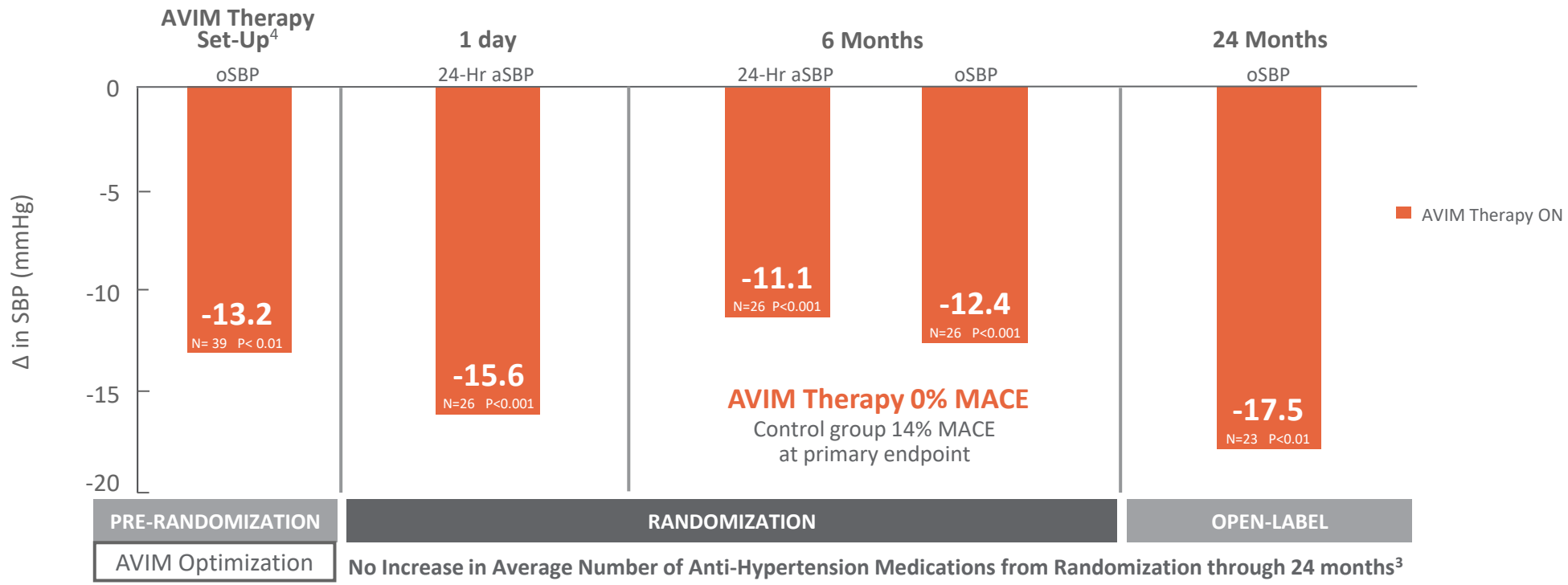
MODERATO II: Compelling Results

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).

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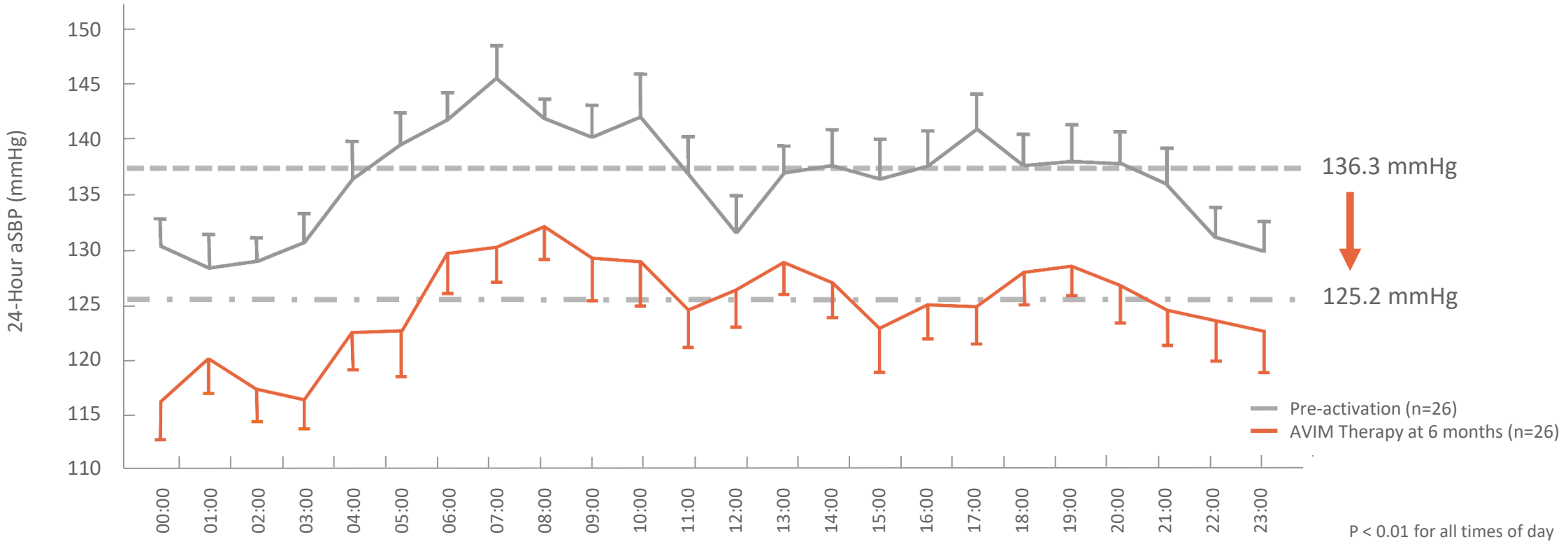
MODERATO II: Reduced Hourly Ambulatory Blood Pressure at 6 Months

Significant Reduction in 24-Hour aSBP 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).

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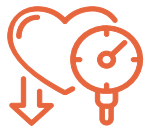
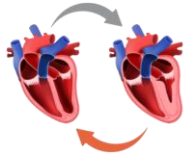
MODERATO II: Evidence of Reduced Pulse Pressure, Improved Diastolic Dysfunction, and Reverse Remodeling

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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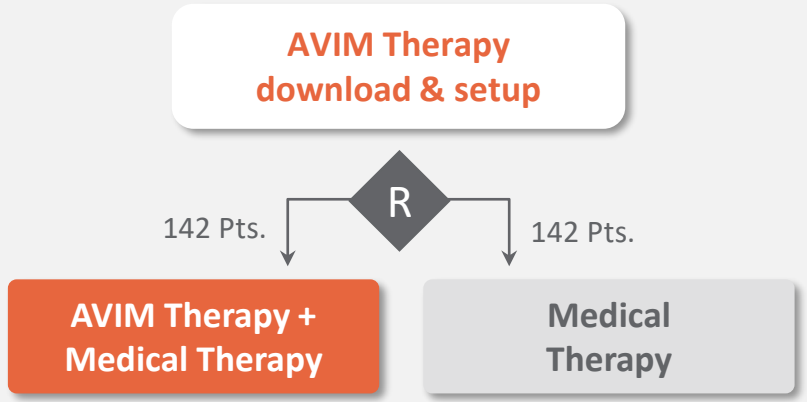
The BACKBEAT Study – Global Pivotal Hypertension Trial

Targeting completion of enrollment by end of Q3 2026 & submitting data for a 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

Virtue® SAB

- Virtue Sirolimus AngioInfusion Balloon (SAB)

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

Designed to provide protected delivery **of gold standard drug to the artery during angioplasty** and maintain required drug levels through critical 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

Rapidly unfolding **paradigm shift to "leave-nothing-behind" treatment with drug-eluting balloons (DEB)** creates high-growth opportunity in large $10B established market[1]

Coronary

~3,700,000 patients

>$7.5 Billion

Peripheral

~1,250,000 patients

>$2.5 Billion

All current DEBs are **drug coated balloons (DCBs) predominantly using paclitaxel**

New clinical evidence supports **DEBs as non-inferior to drug-eluting stents** for de novo coronary disease

AGENT PCB U.S. commercialization **indicates positive sales growth**

Multibillion dollar market for additional **potential vascular indications**

Enhanced reimbursement supports highly attractive U.S. commercial opportunity

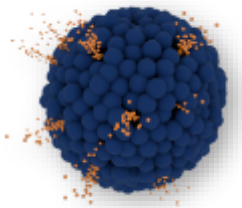
[1]Total addressable market based on company estimates; Definitions: Coronary Artery Disease (CAD), Peripheral Artery Disease (PAD); Drug-eluting balloon (DEB), Drug-coated balloon (DCB), Paclitaxel-coated balloon (PCB)

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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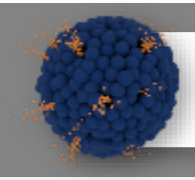
Virtue® SAB – Optimal Drug, Dose and Delivery

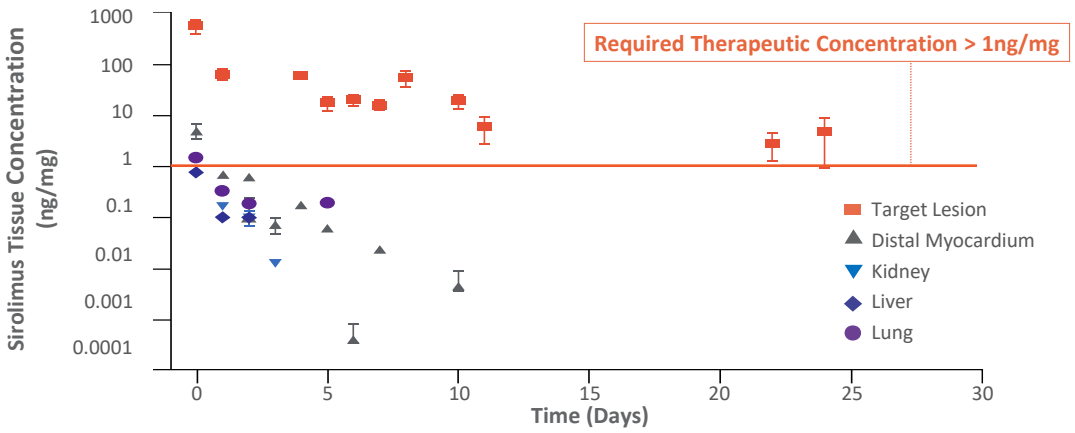


SirolimusEFR™

Protected Delivery of Extended Release Sirolimus

Microporous AngioInfusion™ Balloon

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

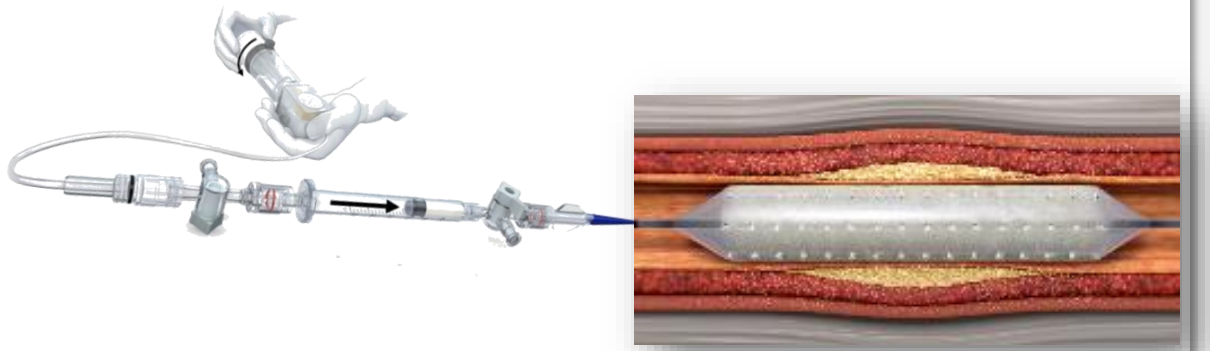


N = 753
porcine coronary artery segments

[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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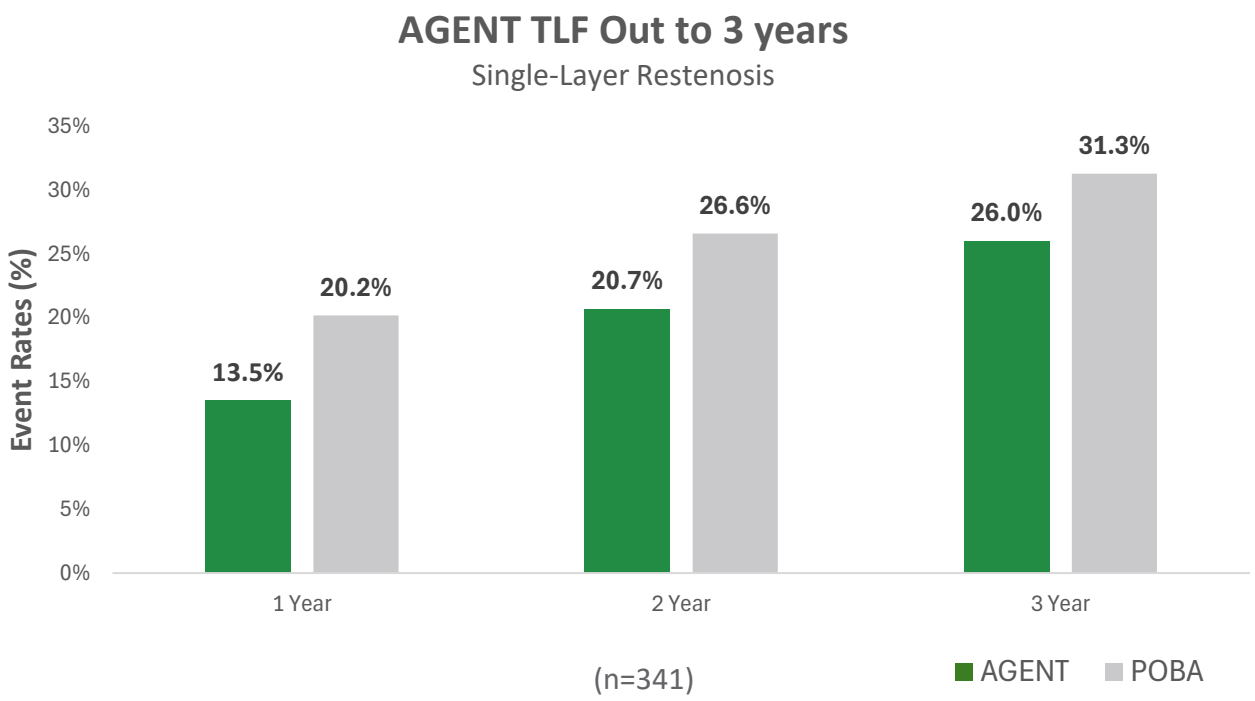
AGENT IDE Trial Results Show Clear Opportunity for Virtue SAB

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

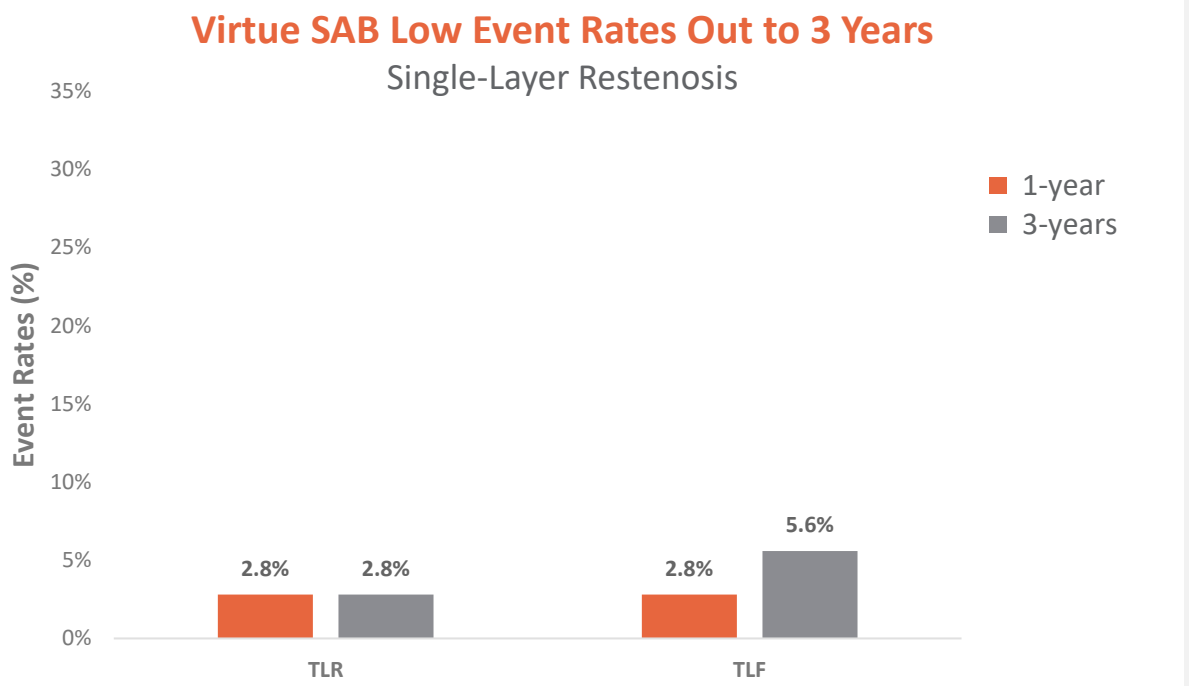
AGENT 93% relative increase in TLF from 1 to 3 years

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]



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

0% Target Lesion Revascularization (TLR) between 1-3 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.
Definitions: Target lesion failure (TLF), late lumen loss (LLL), target lesion revascularization (TLR) and Myocardial Infarction (MI).

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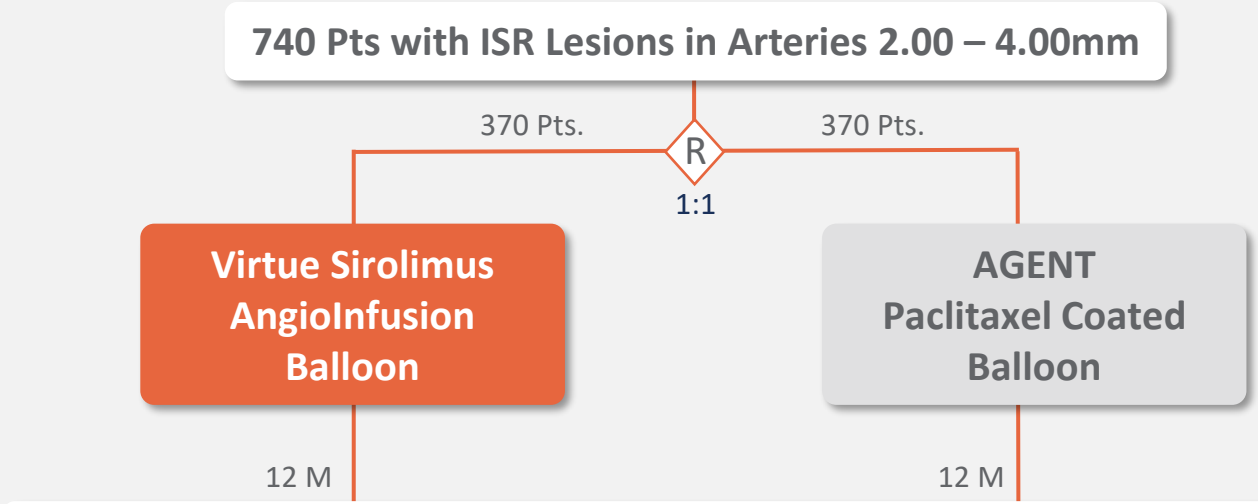
The Virtue Trial – U.S. Pivotal Coronary ISR Trial

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

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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
		HTN with Increased CV Risk (Non-pacemaker indicated)		FDA Breakthrough	
		HTN & Heart Failure	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.

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Leveraging Partnerships to Bring Innovation to Patients & Yield Exceptional Profitability

Partnership-Driven Commercialization with Substantial Royalty-Based Revenue Model

Addressing Major Cardiovascular Indications in Large, Established Global Markets with Unmet Clinical Need

Funded Through Key Upcoming Milestones for AVIM Therapy and Virtue SAB Programs

BACKBEAT Trial
Targeting completion of enrollment by end of Q3 2026 & late-breaking data presentation in Q2 2027*

Virtue Trial
Enrollment ongoing & targeting completion in 2027

*assuming primary endpoints are met

Bringing Medical Innovations to Life Through Partnerships

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