Orchestra BioMed

Corporate Overview

April 2026

Nasdaq: OBIO

Forward-Looking Statements

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Certain statements included in this document that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements relating to the potential safety and efficacy of our product candidates, the initiation, enrollment and timing of our planned pivotal trials and reporting of top-line results, expected market sizes for our product candidates, the ability of our partnerships to accelerate clinical development and the benefits of Breakthrough Device Designation. These statements are based on various assumptions, whether or not identified in this document, and on the current expectations of the Company's management and are not predictions of actual performance. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as and must not be relied on as a guarantee, an assurance, a prediction, or a definitive statement of fact or 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 2026 Vision

Leveraging Partnerships to Bring Innovation to Patients & Yield Exceptional Future Profitability

Actively Enrolling Pivotal Trials for Two High-Impact Proprietary Programs: *AVIM Therapy* and *Virtue SAB*

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

Partnership-Driven Commercialization with Substantial Royalty-Based Revenue Model

Funded Through Completion of Enrollment in *Both* Pivotal Trials and *AVIM Therapy* Primary Endpoint Data Readout

Two Pivotal Trial-Stage Flagship Technologies

Targeting Major Global Unmet Needs in Cardiovascular Disease

AVIM Therapy

Cardiac pacing-based **hypertension** treatment

- Patented therapy delivered as pacemaker firmware enhancement, designed to drive **immediate, substantial and sustained blood pressure reduction**
- Actively enrolling **BACKBEAT Global Pivotal Trial** for uncontrolled hypertension in pacemaker-indicated patients
- **Granted FDA Breakthrough Device Designation** for uncontrolled hypertension in patients with increased cardiovascular risk*

>$17 billion
Annual global
hypertensive heart disease
market opportunity

Strategic Collaboration
Medtronic
Double-digit revenue share

Virtue SAB

Extended-release sirolimus treatment for **artery disease**

- First-of-its-kind **non-coated drug delivery** system designed to deliver large liquid dose of **proprietary extended-release SirolimusEFR™ during angioplasty**
- Actively enrolling **the US pivotal Virtue Trial** randomizing vs. Boston Scientific's AGENT paclitaxel-coated balloon
- **Granted FDA Breakthrough Device Designation** for the treatment of coronary ISR, coronary small vessel disease and below-the-knee peripheral artery disease

>$10 billion
Annual global
atherosclerotic artery disease
Market opportunity

Strategic Rights Agreement
TERUMO
Coronary market ROFR

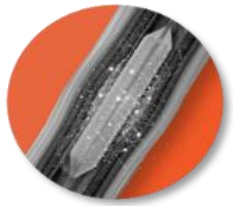
*The U.S. FDA granted Breakthrough Device Designation for an implantable system (i.e., a pacemaker) to deliver AVIM Therapy using conduction system pacing to reduce blood pressure in patients with increased ten-year atherosclerotic cardiovascular disease risk, preserved left ventricular systolic function,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

Recent Accomplishments and Expected 2026-2027 Major Catalysts

AVIM Therapy

- ✓ Received broad FDA Breakthrough Device Designation for uncontrolled hypertension in patients with increased CV risk
- ✓ Updated BACKBEAT global pivotal study protocol to significantly expand eligibility
- ○ Complete BACKBEAT study enrollment
- ○ BACKBEAT study primary efficacy & safety data readout

Virtue SAB



- ✓ Secured FDA IDE clearance and launched the Virtue Trial in coronary ISR
- ✓ Entered into new strategic rights (ROFR) agreement with Terumo
- ○ Complete Virtue Trial study enrollment

Corporate

- ✓ Secured cash runway into Q4 2027 primarily through strategic transactions with Medtronic, Ligand, and Terumo
- ✓ Received initial tranche of cash proceeds (up to $21M expected) from Haemonetics' acquisition of Vivasure Medical
- ○ Receive $35 million in committed tranche payments from Medtronic and Ligand

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

- 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 Designation 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

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**
- Integrated AVIM Therapy for download into premium commercial pacemakers for the BACKBEAT study
- Exclusive global commercial rights for pacemaker-indicated HTN patients; **recent expansion** for future leadless pacemakers
- **Right of first negotiation** to expand global rights for the treatment of **non-pacemaker patients with HTN**

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

[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

AVIM Therapy is a Novel Investigational Treatment for Uncontrolled Hypertension

Designed to Have an Immediate, Substantial, and Sustained Effect[1]

Short AV intervals: Reduce cardiac preload, **immediately lowering blood pressure**

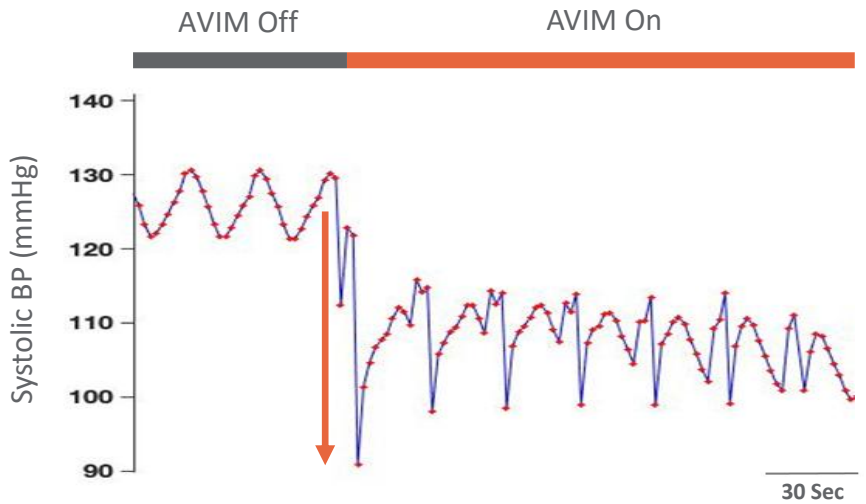
Intermittent longer AV intervals: modulate autonomic nervous system response (baroceptor reflex) and reduce afterload (total peripheral resistance), **sustaining blood pressure reduction**

Utilizes well-characterized physiologic mechanisms (Frank-Starling) to **favorably impact circulatory hemodynamics**[2]:

- Reduces intra-cardiac volumes and pressures
- Improves cardiovascular efficiency
- No adverse impact on contractility

Independent of lead position: compatible with traditional RV pacing or **conduction system pacing**

Novel & Potent Mechanism



[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, Technology and Heart Failure Therapeutics Meeting 2024 **Definitions**: AV (Atrioventricular), RV (Right Ventricular)

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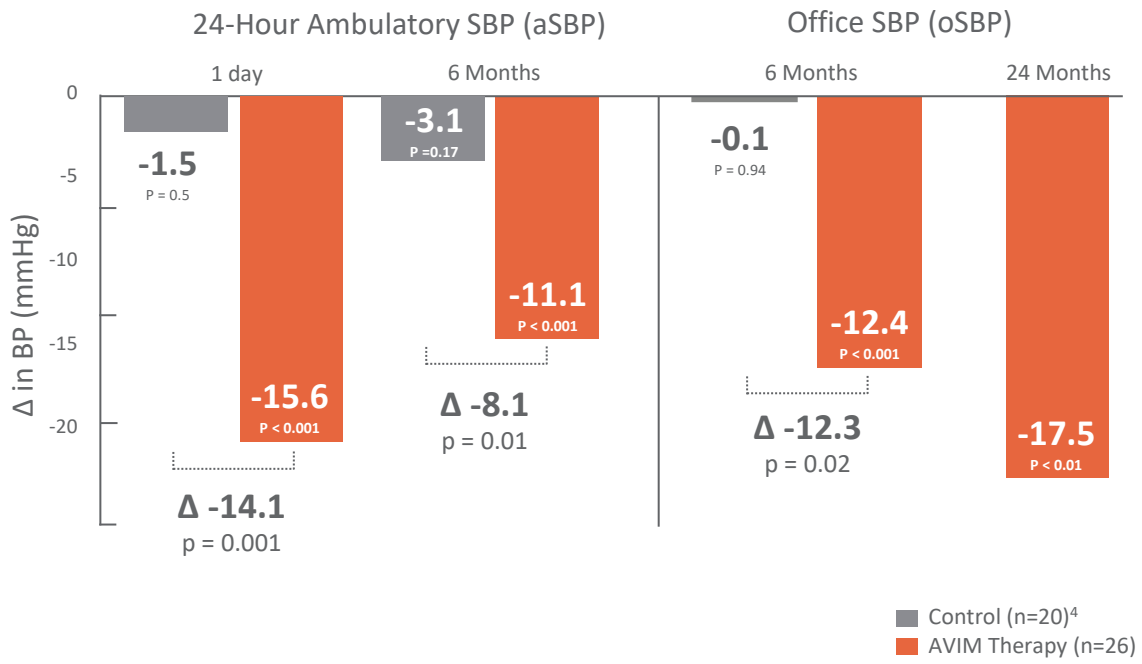
MODERATO II Randomized, Double-Blind Results

Reductions of 10 mmHg in oSBP decrease the relative risk of major cardiovascular events and conditions by over 20%[1]

AVIM Therapy showed encouraging results in MODERATO II, a prospective, multi-center, randomized, controlled, double-blind, pilot study of pacemaker patients with uncontrolled hypertension despite medical therapy[2,3]

Significant Reduction in Systolic Blood Pressure (SBP)



Substantial -11.1 mmHg Reduction
in 24-Hour aSBP at 6 months

0% Major Adverse Cardiac Events
vs. 14.3% in control group at 6 months[5]

Sustained -17.5 mmHg Reduction
in oSBP at 2 years

[1]Ettehad et al. Lancet. 2016;387(10022):957–967. doi:10.1016/S0140-6736(15)01225-8. [2]Kalaras et al. Journal of the American Heart Association. 2021;10:e020492 ahajournals.org/doi/10.1161/JAHA.120.020492; [3]Burkhoff MODERATO II Study 2-Year Results TCT 2021; [4]24-Hr aSBP Control (n=19), 1 control patient could not be measured despite repeat measurement (patient had extremely high blood pressure); [5]A blinded evaluation Data Safety Monitoring Board report for MODERATO II included a revised MACE rate, from 9.5% to 14.3%, in the control group to reflect a heart failure after publication of the study results. **Definitions**: Major Adverse Cardiac Events (MACE) included death, heart failure, clinically significant arrhythmias (i.e., persistent or increased atrial fibrillation, serious ventricular arrhythmias), myocardial infarction, stroke and renal failure in treatment group calculated per patient.

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Favorable Impact on Hypertensive Heart Disease

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

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

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

– 9.5 mmHg
in 24-Hour aSBP
at 6 months

– 15.8 mmHg
in oSBP
at 2 years

– 9.6 mmHg
Δ in Ambulatory PP
at 6 months

– 13.9 mmHg
Δ in Office PP
at 2 years

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

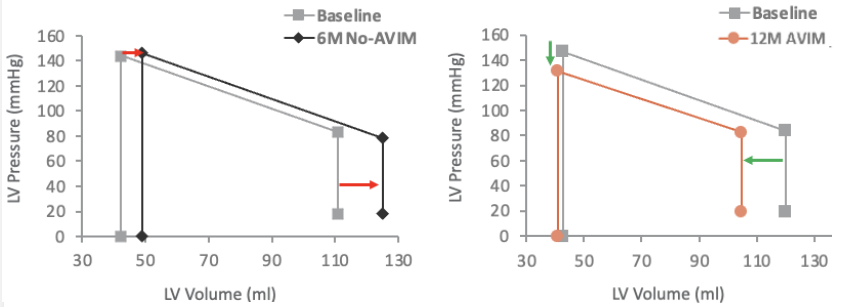
Improved Diastolic Dysfunction (DD) In Echocardiographic Analysis[4]

>61% of AVIM Therapy patients in MODERATO II had DD

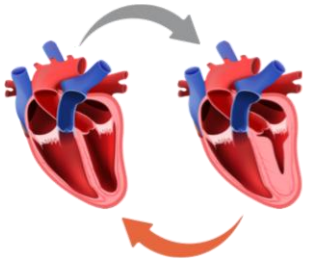
- AVIM therapy **significantly reduced SBP** in patients with and without DD
- AVIM therapy **improved myocardial relaxation and improved diastolic compliance** (significantly increased e' and E/A)

Retrospective, treatment-blinded analysis of core lab echocardiograms from MODERATO II, hypertensive pacemaker patients with LVEF ≥ 50% and NYHA class < II, with independent blinded adjudication

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



Control Group Developed Ventricular Remodeling



AVIM Therapy Induced Reverse Remodeling

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

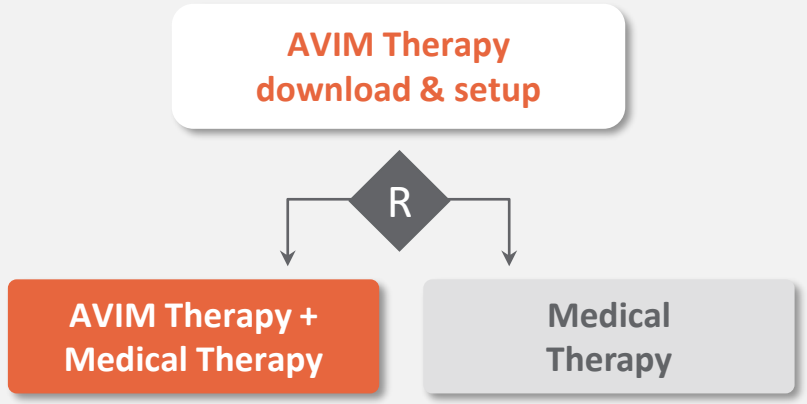
The BACKBEAT Study – Global Pivotal Hypertension Trial

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

BACKBEAT
GLOBAL PIVOTAL STUDY

- Randomized, prospective, multi-center, double-blind, controlled trial
- Up to 500 patients across 130 sites in U.S., EU & APAC countries
- 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

Virtue 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

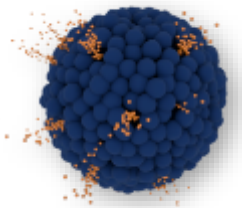
[1]Total addressable market based on company estimates; Definitions: Coronary Artery Disease (CAD), Peripheral Artery Disease (PAD); Drug-eluting balloon (DEB), Drug-coated balloon (DCB), Paclitaxel-coated balloon (PCB)

Compelling Opportunity 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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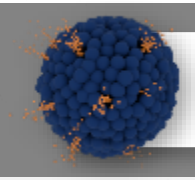
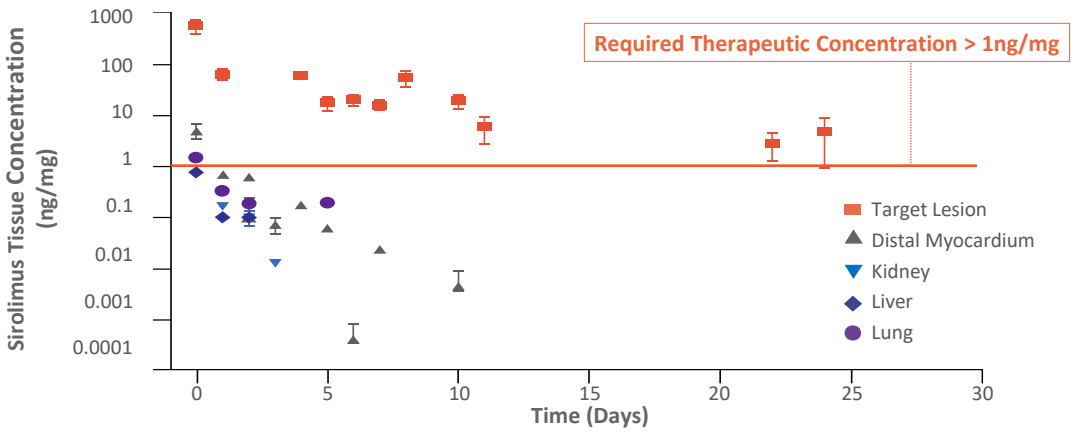
Virtue® SAB – Optimal Drug, Dose and Delivery



SirolimusEFR™ | **Protected Delivery of Extended Release Sirolimus** | **Microporous AngioInfusion™ Balloon**

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

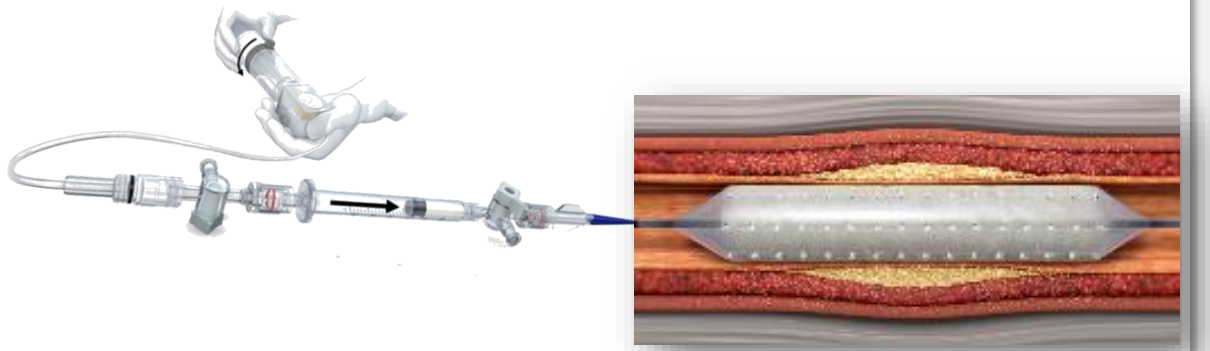


N = 753
porcine coronary artery segments

[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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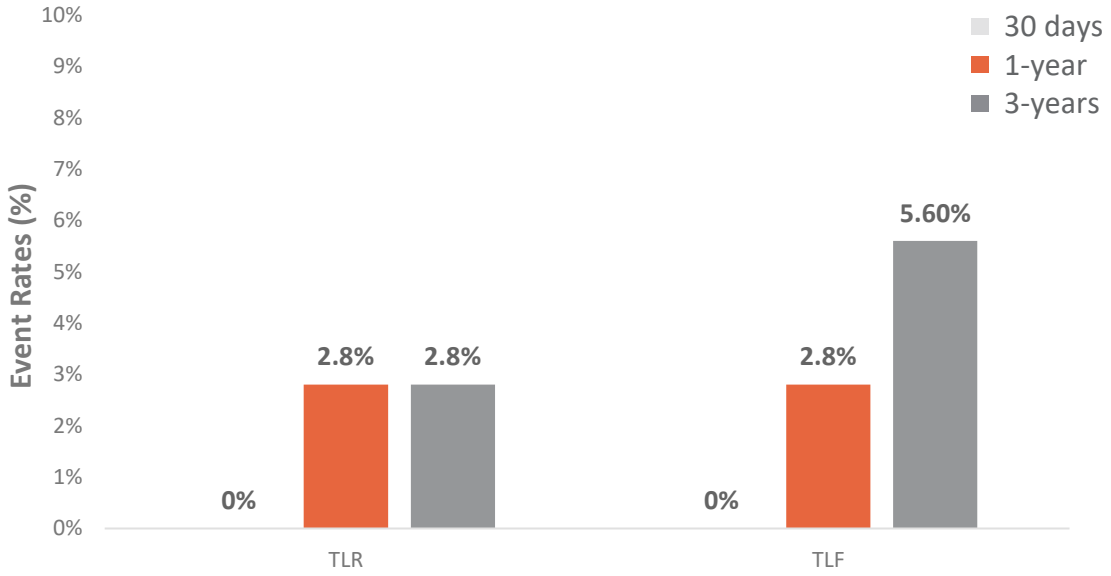
Compelling SABRE Trial Results in Coronary ISR Patients

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]

Virtue SAB Low Event Rates Out to 3 Years

Single-Layer Restenosis



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

2.8% Cardiac Death and 0% TV-MI at 3-years

[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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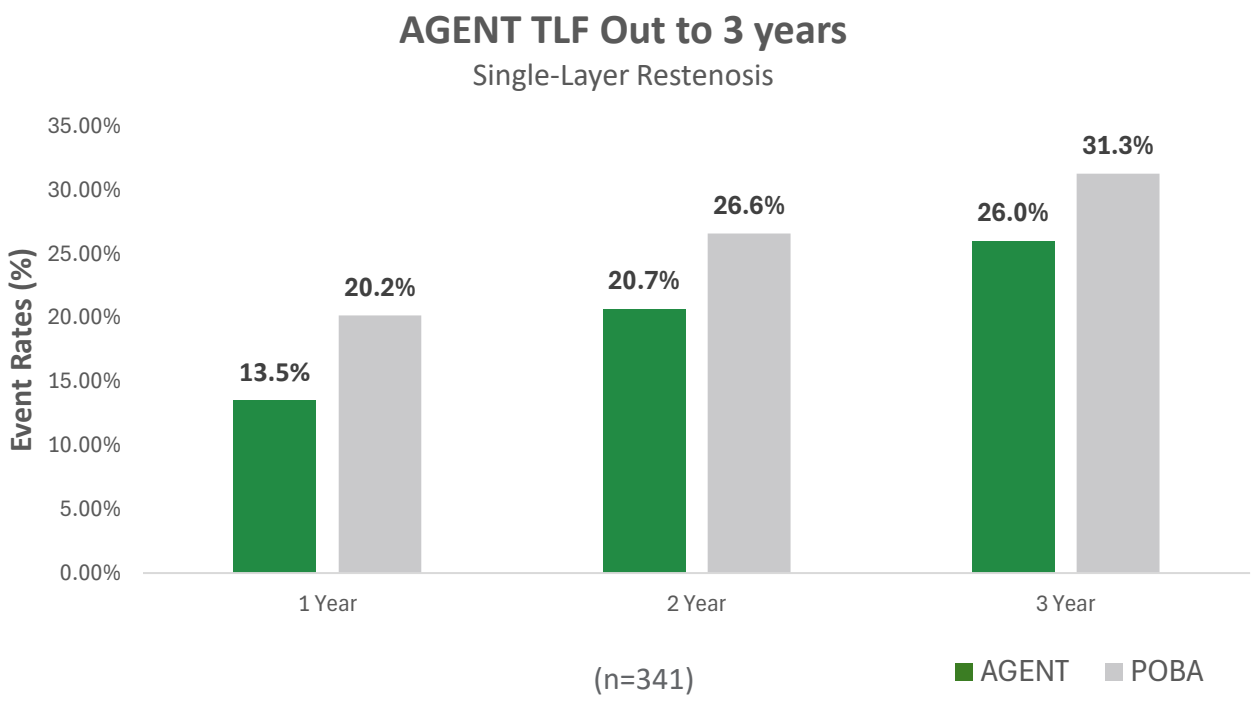
AGENT IDE Trial Results Show Clear Opportunity for Virtue SAB

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)

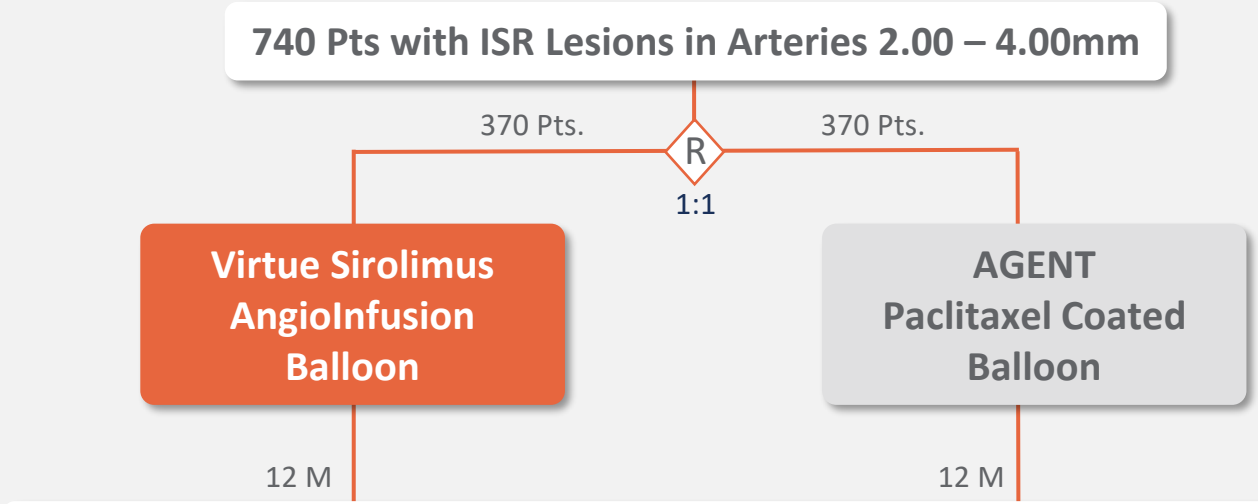
The Virtue Trial – U.S. Pivotal Coronary ISR Trial

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
- Up to 75 US Sites
- 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

Orchestra BioMed™

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 Future Profitability

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

Partnership-Driven Commercialization with Substantial Royalty-Based Revenue Model

Funded Through Completion of Enrollment in Both Pivotal Trials and *AVIM Therapy* Primary Endpoint Data Readout

Bringing Medical Innovations to Life Through Partnerships

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