Orchestra BioMed

Corporate Presentation

December 2024

Forward-Looking Statements

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

Certain statements included in this document that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements relating to the potential safety and efficacy of our product candidates, the initiation 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 our estimated future financial performance and financial position. 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 27, 2024 as updated by any risk factors disclosed under the heading "Item 1A. Risk Factors" in 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 Executive Overview

Partnership-Enabled Business Model Designed to
Accelerate Innovation to Patients & Yield Exceptional Future Profitability

Atrioventricular Interval Modulation (AVIM) Therapy

- **$10B** annual hypertension target market
- Statistically significant efficacy data from double-blind, randomized pilot study
- BACKBEAT global pivotal study enrollment underway

Medtronic

Strategic collaboration

Double-digit revenue share

Virtue® Sirolimus AngioInfusion Balloon (SAB)

- **$4B** annual artery disease target market
- Strong safety & efficacy data out to 3 years in multi-center pilot study
- Conditional IDE approval received for coronary pivotal study

TERUMO

Strategic collaboration

Double-digit revenue share

Orchestra BioMed™

Orchestra BioMed's Partnership-Enabled Model Benefits All

Orchestra BioMed
Development

- Secure substantial long-term royalties
- Outsource commercialization
- Enable multiple pipeline opportunities

Shared Benefits
Innovation

- Improve patient lives
- Accelerate development
- Leverage expertise & resources

Strategic Partners
Commercialization

- Enable new growth opportunities
- Outsource development
- Minimize P&L dilution

Advancing High-Impact Pipeline*

Product Platforms	Target Indications	Preclinical	Clinical Feasibility	Clinical Pivotal	Partner
AVIM Therapy (also known as BackBeat CNT™)	**Hypertension (HTN)** (pacing patients; HTN+P)	BACKBEAT Global Pivotal Study Enrolling			Medtronic
	High-Risk HTN (non-pacing patients)				ROFN: Medtronic
CNT - HF	Heart Failure				
Virtue® Sirolimus AngioInfusion™ Balloon (SAB)	**Coronary In-Stent Restenosis (ISR)**	IDE Approved[1] & FDA Breakthrough			TERUMO
	Coronary Small Vessel (SV)[1]	FDA Breakthrough			TERUMO
	Below-the-Knee (BTK)[1]	FDA Breakthrough			TERUMO
SirolimusEFR™ / Microporous Balloon	Ortho, oncology, urology, GI & other				

*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, 2023 filed with the SEC on March 27, 2024, as updated by our subsequently filed quarterly reports on Form 10-Q; [1]In light of the recent FDA approval of Boston Scientific Corporation's AGENT™ paclitaxel-coated balloon for the treatment of coronary ISR, we and Terumo are reviewing the design for the Virtue ISR-US pivotal study and considering alternative clinical study designs with input from our clinical steering committee for Virtue SAB

Orchestra BioMed™

Highly Accomplished Executive Team & Board

David Hochman

Chairman, CEO, Founder

Darren R. Sherman

President, COO, Director, Founder

Andrew Taylor

Chief Financial Officer

Yuval Mika, Ph.D.

GM & CTO, Bioelectronic Therapies

George Papandreou, Ph.D.

GM & SVP, Focal Therapies

Bill Little

EVP, Corporate Development & Strategy

Hans-Peter Stoll, M.D., Ph.D.

Chief Clinical Officer

Avi Fischer, M.D.

SVP, Medical Affairs & Innovation

Bob Laughner

SVP, Regulatory & Quality

Juan Lorenzo

SVP, Product Development, Focal Therapies

Executive Team: | >300 Years of Experience | >25 Avg Industry Years Each | >100 Product Approvals | >600 Authored Patents

Independent Board Members

Jason Aryeh

Pamela Connealy

Eric S. Fain, M.D.

Eric A. Rose, M.D.

David Pacitti

John Mack

Atrioventricular Interval Modulation (AVIM) therapy

Also known as BackBeat CNT™

AVIM Therapy Overview

Collaboration with Medtronic

Risk of High Blood Pressure

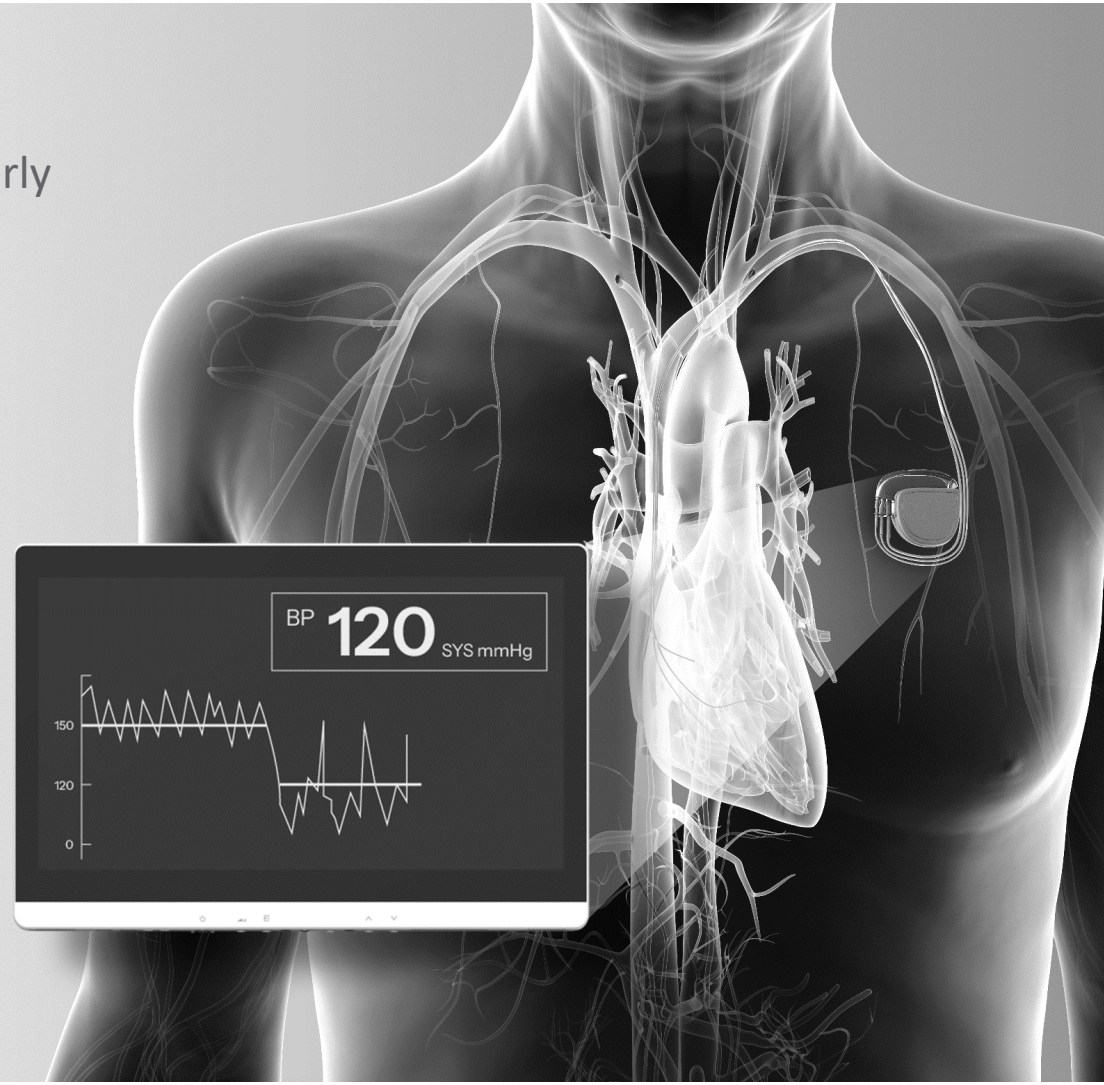
Hypertension is the **leading global risk factor for death,** particularly for **older, higher risk patients,** despite pharmacotherapy

Novel Therapy

Pacemaker-delivered therapy designed to **immediately, substantially and persistently reduce blood pressure**

Immediate Unmet Patient Need

Initial treatment target is existing pacemaker population for whom **hypertension is the #1 comorbidity**



Orchestra BioMed

Large Global Opportunity for Treating Hypertension in Target Populations*

HTN + Pacemaker

750,000 patients

~70% of pacemaker patients[1]

>$2 Billion

High Risk HTN

2,400,000 patients

~0.2% of HTN patients

>$8 Billion

- Same patients, device implant, and treating physicians
- Existing reimbursement structure

- Older patients with uncontrolled hypertension and other significant comorbidities
- Similar demographics to pacemaker patients, high-risk, difficult-to-treat

*Total addressable market in 2025 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)

Orchestra BioMed™

AVIM Therapy Strategic Collaboration with Medtronic

- **Developed AVIM therapy** (BackBeat CNT) **from concept stage**
- Owns all related intellectual property: **over 110 issued global patents**
- 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]

- Global market leader in cardiac pacing therapy: **>$1.5B in annual revenues**
- Integrated AVIM therapy for download into premium commercial pacemakers for the BACKBEAT study
- Exclusive global commercial rights for AVIM therapy in pacemaker-indicated patients with HTN
- Right of first negotiation to expand global rights for the treatment of non-pacemaker patients with HTN
- **$50M equity investment** 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

AVIM Therapy Substantially and Persistently Reduces Blood Pressure Through a Novel Mechanism of Action

AVIM therapy uses a dual-chamber pacemaker to deliver repeated sequences of **short and longer AV intervals**[1] to reduce blood pressure by:

Short AV Intervals: Reduce cardiac preload, immediately lowering blood pressure

Longer AV Intervals: Modulate autonomic nervous system responses (sympathetic tone) and reduce afterload (Total Peripheral Resistance), sustaining the 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

Compatible with traditional RV lead locations or **conduction system pacing**

[1]Kalaras 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

Orchestra BioMed™

Existing Body of Clinical Data Supporting Efficacy and Safety

2012

Feasibility Study in Canine HTN Model
Proof of concept

Acute Feasibility Study in Subjects with HTN

2016

MODERATO I - First In-Human Implant Study
Multi-center, Single-arm Study

TCT Innovation Shark Tank Award
Cardiovascular Research Foundation®

Best Abstract at ICI

2019

MODERATO II – Pilot Study
Prospective, multi-center, randomized, controlled, double-blind pilot study;
Primary endpoint data late-breaking presentation at TCT
Cardiovascular Research Foundation®

2021

MODERATO II Two-year and ISH results
Presented at TCT
Cardiovascular Research Foundation®

Peer-Reviewed Publication of MODERATO II Results
in the Journal of the American Heart Association
American Heart Association.

2022

Strategic Partnership with Medtronic
for development and commercialization of AVIM therapy for hypertensive pacemaker patients
Medtronic

2024

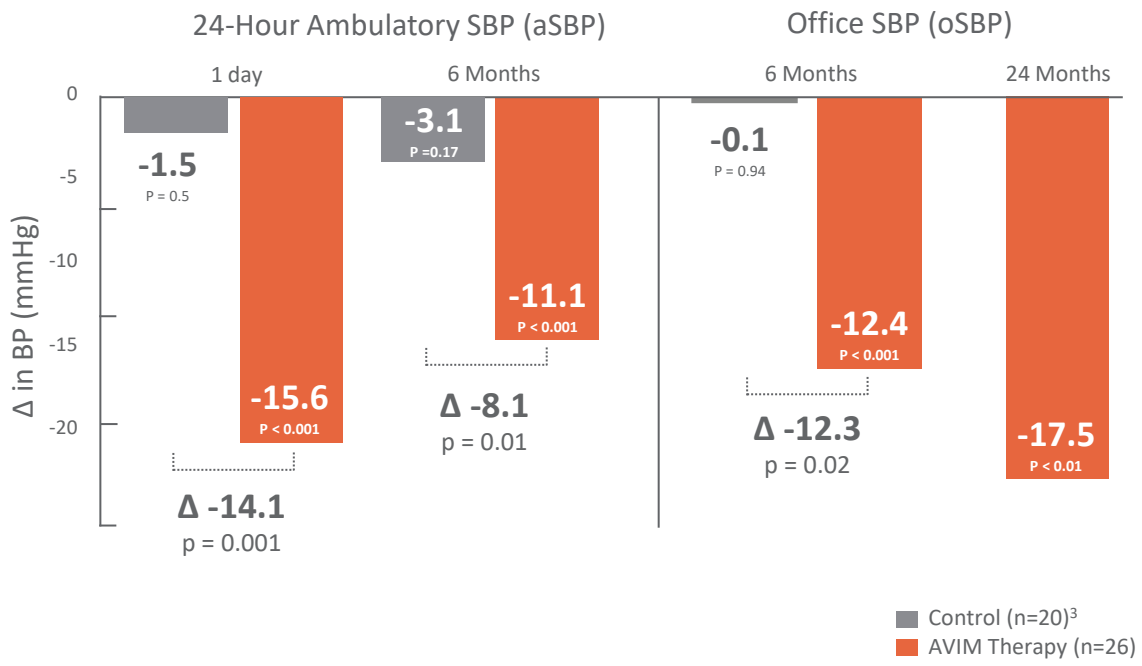
Enrolling BACKBEAT Pivotal Study
Prospective, multi-center, randomized, controlled, double-blind pivotal study

Orchestra BioMed™

MODERATO II Randomized, Double-Blind Results

AVIM Therapy showed encouraging results in MODERATO II, a prospective, multi-center, randomized, controlled, double-blind, pilot study of pacemaker patients with persistent uncontrolled hypertension despite medical therapy[1,2]

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[4]

Sustained -17.5 mmHg Reduction
in oSBP at 2 years

[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]24-Hr aSBP Control (n=19), 1 control patient could not be measured despite repeat measurement (patient had extremely high blood pressure); [4]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.

Orchestra BioMed™

BACKBEAT Study Objective and Design

Study objective: Evaluate the safety and efficacy of AVIM therapy in subjects indicated for a dual-chamber pacemaker who have uncontrolled hypertension (HTN) despite the use of antihypertensive medications

Enroll approximately **500 patients across up to 100 study sites** in the US and Europe

Randomized (1:1) double-blind clinical trial

- Treatment Group: AVIM therapy + continued anti-HTN drug therapy
- Control Group: AVIM therapy not activated + continued anti-HTN drug therapy

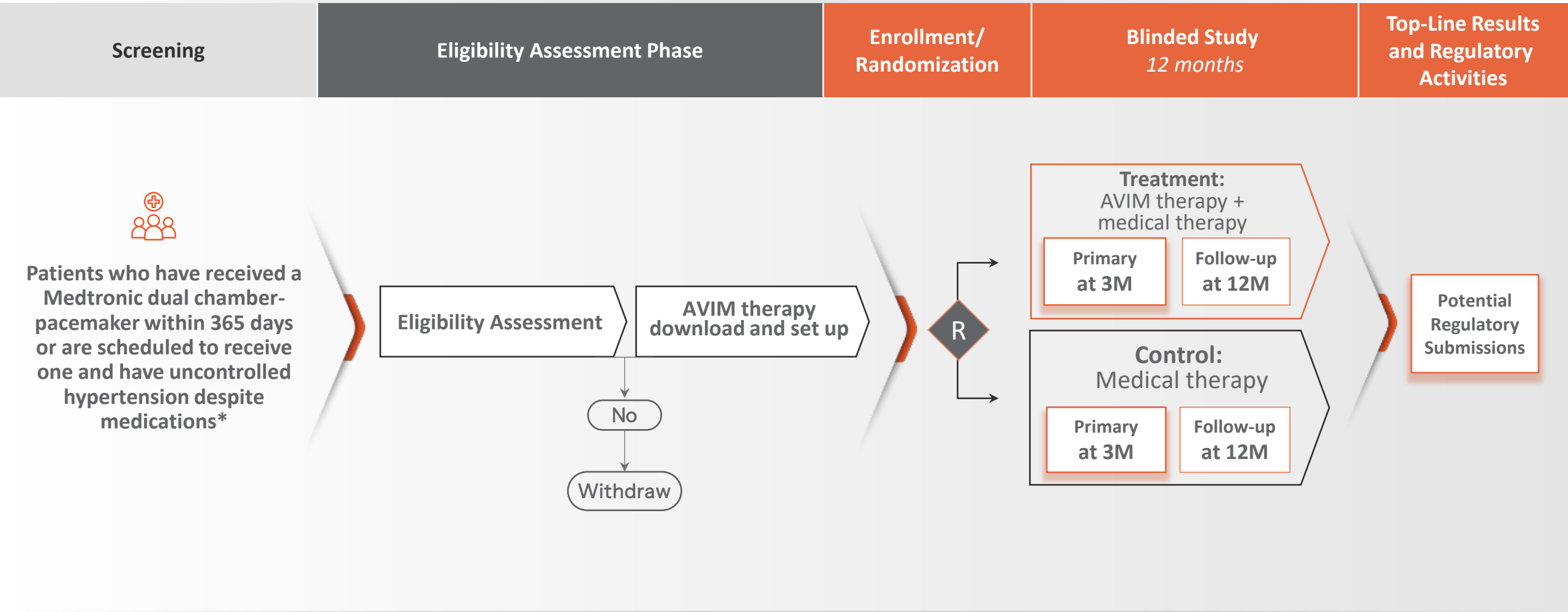
Study endpoints:

- **Primary Efficacy endpoint:** Between group difference in the **change of mean 24-hour aSBP at 3 months** post randomization
- **Primary Safety endpoint:** Freedom from **unanticipated serious adverse device events at 3 months** post randomization
- **Secondary/additional endpoints**: Double-blind follow up will continue through 12 months to enable collection of additional clinical results and the secondary safety endpoint (CCAE rate)

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed™

BACKBEAT Study Design



*Implant is decoupled from study outcomes & endpoints

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed™

Virtue® Sirolimus AngioInfusion™ Balloon (SAB)

Virtue® SAB Overview

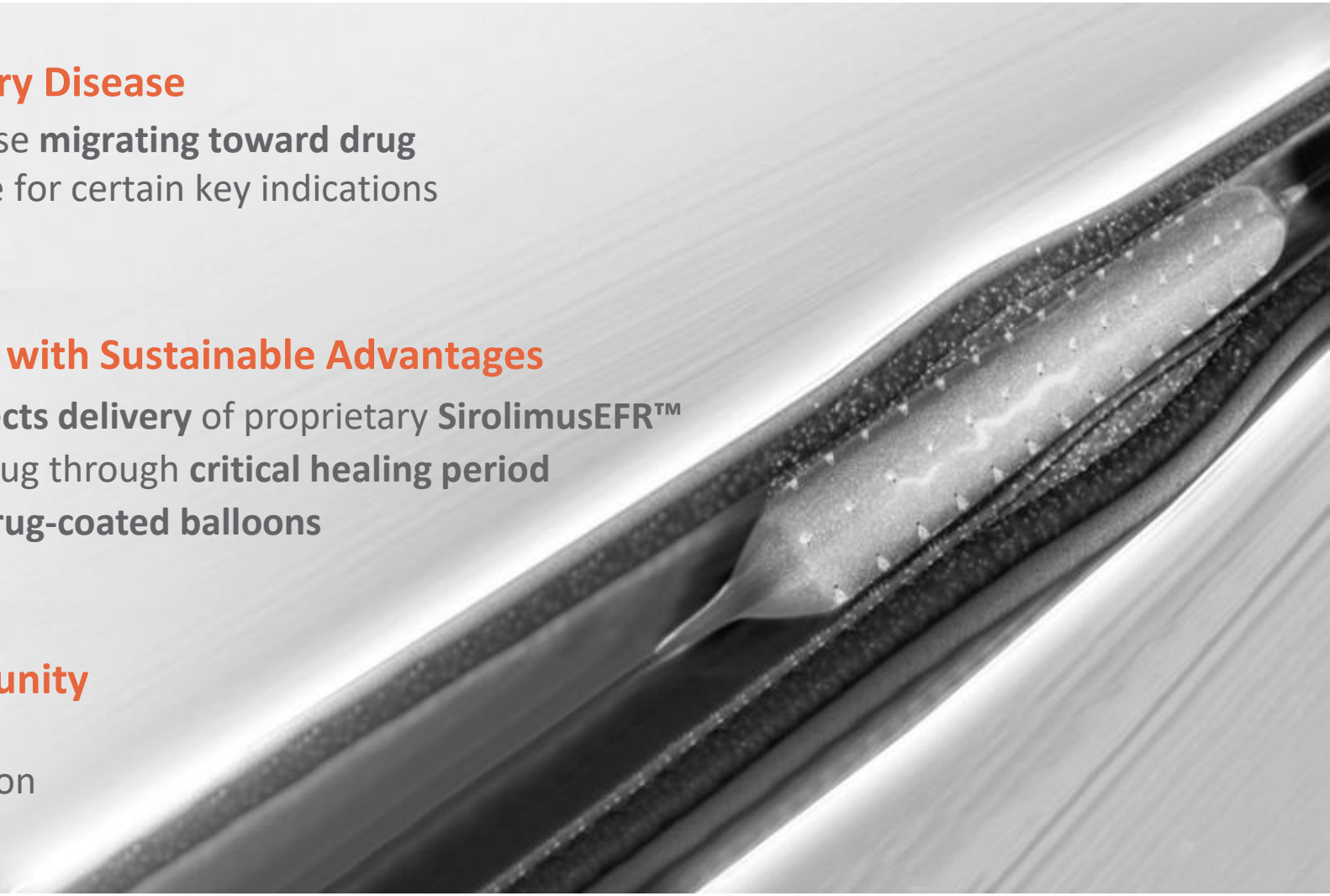
Collaboration with TERUMO

Paradigm Shift in Treatment of Artery Disease

Interventional treatment of artery disease **migrating toward drug coated balloons** as new standard of care for certain key indications

Highly Differentiated Sirolimus DEB with Sustainable Advantages

- **Non-coated** microporous balloon **protects delivery** of proprietary **SirolimusEFR™**
- **Extended release** of "gold-standard" drug through **critical healing period**
- Designed to **overcome limitations of drug-coated balloons**



Large Breakthrough Market Opportunity

Over 3M* targeted annual procedures
globally for FDA Breakthrough Designation
in coronary and peripheral indications

*Total addressable market in 2025 based on company estimates

Orchestra BioMed™

Large Global Opportunity for Virtue SAB*

Coronary

~2,000,000 patients

In-stent Restenosis, Small Vessel De Novo

>$2.4 Billion

Peripheral

~1,250,000 patients

Below-The-Knee

>$1.6 Billion

- Large mature market with suboptimal treatments for coronary in-stent restenosis, coronary small vessel de novo and below-the-knee
- Multibillion dollar established market for additional potential vascular indications

*Total addressable market in 2025 based on company estimates; Definitions: Coronary Artery Disease (CAD), Peripheral Artery Disease (PAD)

Strategic Collaboration with Terumo

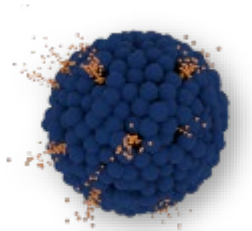
- **Developed Virtue SAB** (SirolimusEFR, AngioInfusion balloon) **from concept stage;** owns all related IP
- Conducted all prior development work including SABRE study in coronary ISR
- Sponsoring the Virtue ISR-US pivotal study (conditional IDE granted)
- **10-15% royalty on net sales PLUS per unit payments** for SirolimusEFR
- Retained rights for all non-vascular indications

- Global leader in interventional cardiology accessory devices: **>$2.4B in annual revenues**[1]
- Completed a **$30M upfront payment** to and $5M equity investment in Orchestra BioMed
- Currently renegotiating $65M in clinical and regulatory milestone payments
- Responsible for clinical/regulatory costs (excluding Virtue ISR-US study), device supply & commercialization
- Potential for Virtue SAB to become Terumo's flagship therapeutic offering

[1]Based on Terumo's consolidated financial results for the fiscal year ended March 31, 2023; Initiation of Virtue ISR-US pivotal study of Virtue SAB for the treatment of coronary ISR, as well as submissions to Japanese PMDA in coronary ISR and small vessel disease are pending ongoing operational and financial plan calibration with Terumo, currently anticipated to conclude in the second half of 2024

Compelling Opportunity For Virtue SAB

A novel solution is required to realize advantages of sirolimus



SirolimusEFR™

+

Microporous AngioInfusion™ Balloon

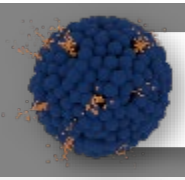
=

Angioplasty with Protected Delivery of Extended Release 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 limitations** including risk of emboli from large coating particulates, drug loss in transit and rapid navigation requirements

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

Virtue® SAB – Optimal Drug, Revolutionary Delivery

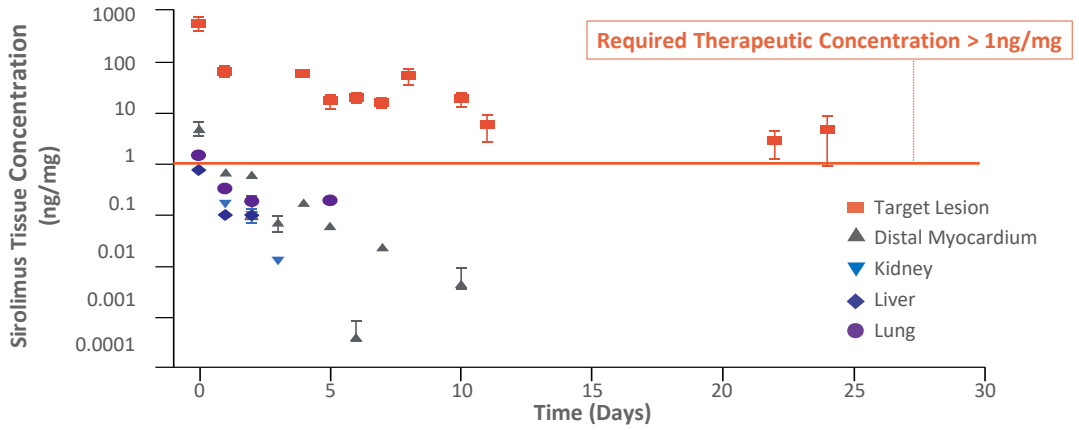


SirolimusEFR™

Protected Delivery of Extended Release Sirolimus

Microporous AngioInfusion™ Balloon

Published Data Demonstrates Therapeutic Sirolimus Tissue Concentration Through Critical Healing Period (~30 Days)



N = 753
porcine coronary artery segments

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

Precise dose loaded and protected in Dose Unit

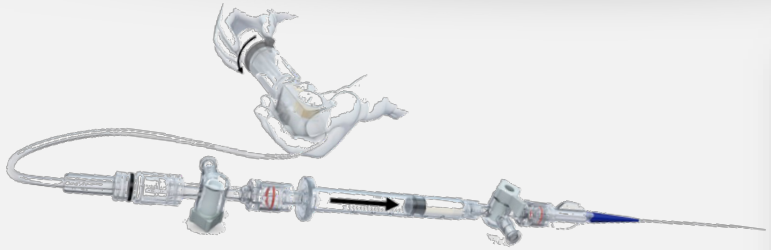
***No coating* = no drug loss in transit**

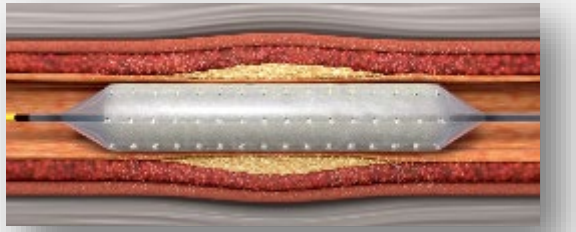
Standard navigation to lesion

***No coating* = no rush to target lesion**

Intended dose delivered through balloon micropores

***No coating* = no large particulate**



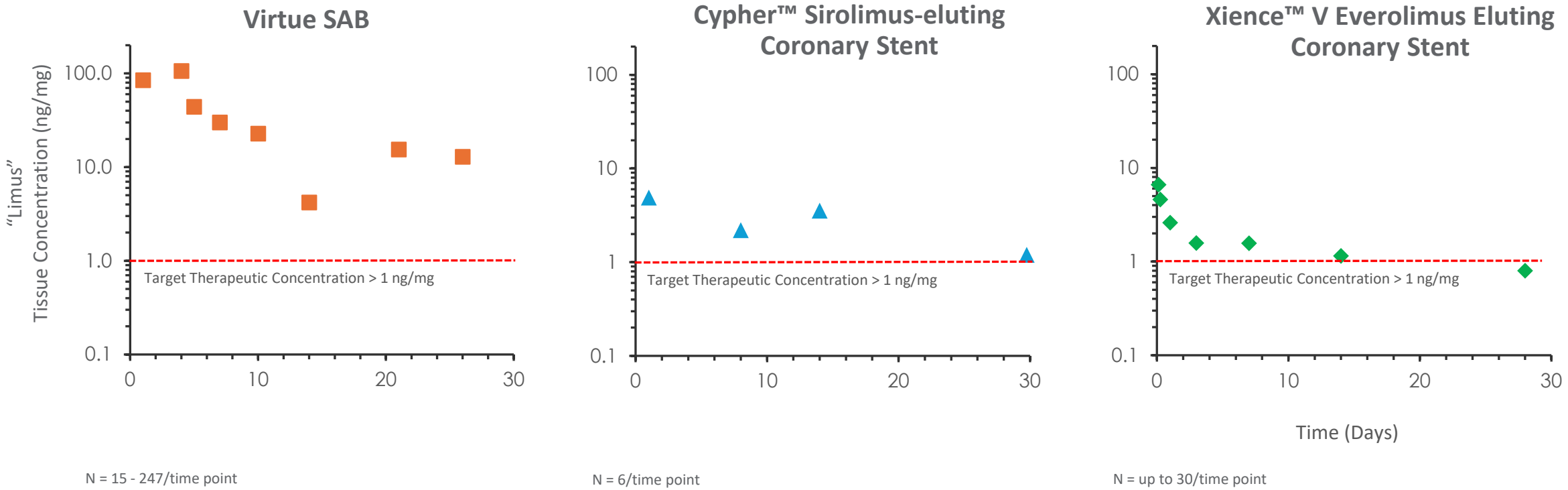


[1]Granada et al. EuroIntervention 2016;12:740-747

Orchestra BioMed™

Virtue SAB Achieves Therapeutic Sirolimus Tissue Concentrations Through the Critical Healing Period

Virtue SAB & Proven DES Achieve Therapeutic Sirolimus Tissue Concentrations Through Critical Healing Period (~30days)



Adapted from 3 separate preclinical porcine studies[1,2,3]

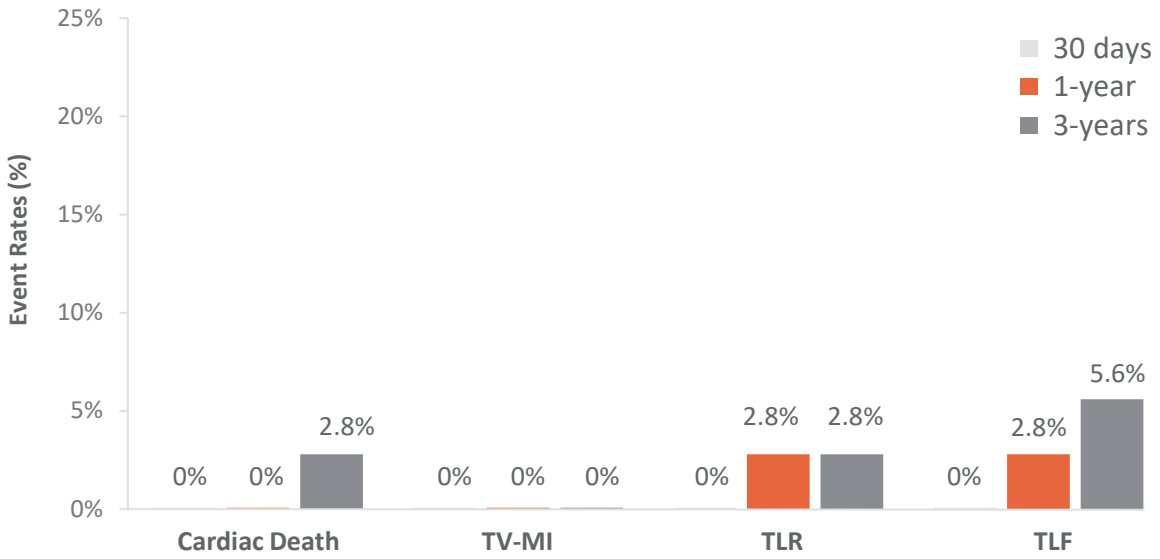
[1]Granada J, et al. EuroIntervention 2016;12:740-747. [2]Balakrishnan et al, J Control Release. 2008, 131(3): 173–180. [3]Perkins et al, J Int Cardiol 2009; 22(Suppl 1): S28-S40. XIENCE V is a trademark of the Abbott Group of Companies. Cypher™ Sirolimus-eluting Coronary Stent is a trademark of Cordis Coporation

Orchestra BioMed™

Compelling SABRE Trial Results in Coronary ISR Patients

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

Low Event Rates Out to 3 Years



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

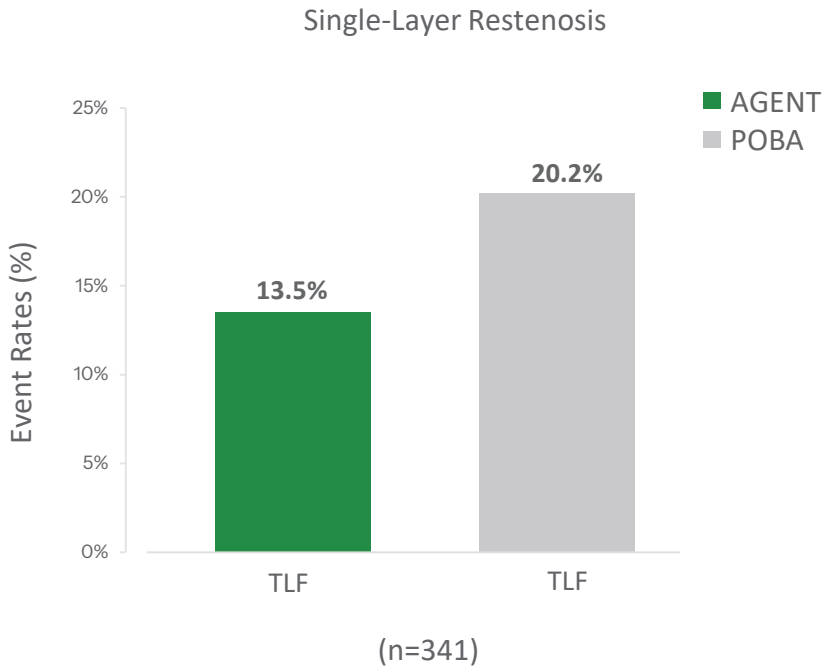
[1]Verheye et al. JACC Cardiovasc Interv 2017 Oct 23;10(20):2029-2037. DOI: 10.1016/j.jcin.2017.06.021. [2] Revised per protocol analysis set meets the criteria of the proposed In-Stent Restenosis IDE study population. ***Definitions:*** Target lesion failure (TLF), late lumen loss (LLL), target lesion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

Orchestra BioMed™

AGENT IDE Results in Single-Layer ISR Patients

AGENT IDE TLF results vs. Plain Balloon Angioplasty (POBA) at 1-year in patients with single-layer restenosis

The AGENT IDE Randomized Clinical Results Out to 1 year[1]



13.5% TLF at 1 year

To date, 1 year follow-up only

No angiographic follow-up

[1]Yeh RW, Shlofmitz R, Moses J, et al. *JAMA.* 2024;331(12):1015–1024. doi:10.1001/jama.2024.136

Orchestra BioMed™

Key Investment Highlights

Lead Partnered Program Enrolling Pivotal Study

- AVIM Therapy is compelling HTN therapy in pivotal study
- Actively enrolling with market-leading strategic partner
- Substantial revenue share with significant follow-on market opportunity

Partnered Program Approved For Pivotal Study

- Virtue SAB is a highly differentiated solution for large existing market
- Conditional IDE-approved for pivotal study
- Significant near-term milestones

Differentiated Business Model

- Enabled by partnerships
- Capital efficient
- Designed to yield exceptional future profitability

Strong Shareholder Base & Financial Runway

Medtronic rtw PERCEPTIVE ADVISORS TERUMO

- Current financial runway estimate: 2H 2026

Orchestra BioMed™

Bringing Medical Innovations to Life Through Partnerships