Orchestra BioMed™

R&D DAY 2026

November 12 | Lotte New York Palace

Orchestra BioMed · Nasdaq: OBIO



R&D Day 2026

Opening Remarks · David Hochman, Chairman & CEO

Orchestra BioMed · Nasdaq: OBIO

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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, the benefits of Breakthrough Device Designation and the Company's projected cash runway. 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.

Recent Business Updates

FUNDED THROUGH

2028

- **$80.5 million net proceeds** from public offering, closed on November 9, 2026
- In addition to **$101.9M in cash**, cash equivalents and marketable securities at September 30, 2026



BACKBEAT ENROLLMENT COMPLETE

349 patients randomized across 92 sites in 15 countries



FDA PMA SUPPLEMENT PATHWAY CONFIRMED

Medtronic to submit after primary data presentation



VIRTUE TRIAL ENROLLMENT ACCELERATING

Targeting completion of enrollment by end of 2027

Key Catalysts: BACKBEAT & Virtue Pivotal Trials

= Dependent on trial outcomes and regulatory/partner timing

COMPLETE

BACKBEAT
Fully enrolled

VIRTUE
Actively enrolling

Q2 2027

BACKBEAT
Present primary endpoint data

2H 2027

BACKBEAT
PMA submission review

VIRTUE
Targeting enrollment completion by end of 2027

1H 2028

BACKBEAT
Potential FDA approval & AVIM Therapy US commercial launch

2H 2028

BACKBEAT
Potential OUS launches

VIRTUE
Potential completion of 12-month primary endpoint follow-up

Today's Agenda & Speakers

3:00 PM

Opening Remarks

David Hochman, Chairman & Chief Executive Officer

3:10 PM

Virtue SAB & Virtue Pivotal Trial

Led by Darren R. Sherman
David Hochman
Duane Pinto, MD, MPH, Senior Clinical Advisor (Orchestra), Chief Medical Officer, JenaValve Technologies, Associated Professor of Medicine, Harvard Medical School

4:20 PM

AVIM Therapy, BACKBEAT Pivotal Trial & Medtronic Strategic Collaboration

Led by David Hochman
Darren R. Sherman, President & Chief Operating Officer

5:15 PM

Q&A and Closing Remarks

Moderated by David Hochman and Darren R. Sherman

PHYSICIAN SPEAKERS

Allen Jeremias, MD — Virtue Trial Co-Principal Investigator; Director of the Cardiac Catheterization Laboratory, St. Francis Hospital & Heart Center, New York

Vivek Reddy, MD — Executive Chairman, BACKBEAT Trial Steering Committee; Director of Cardiac Arrhythmia Services, Mount Sinai Hospital and Mount Sinai Health System

Marat Fudim, MD — Associate Professor of Cardiology, Advanced Heart Failure, Duke University Medical Center

R&D Starts with Patient Unmet Need

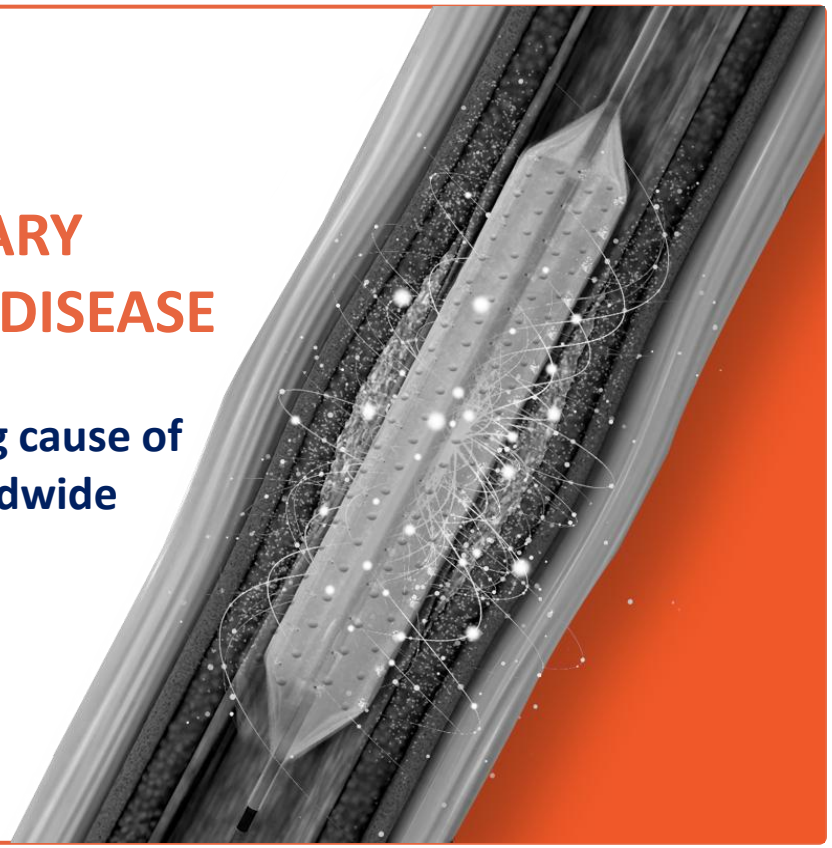
HYPERTENSION

The #1 risk factor for death worldwide



CORONARY ARTERY DISEASE

The leading cause of death worldwide



Orchestrating Innovation: Our Approach to R&D

BUILD ON PROVEN FOUNDATIONS 1

Pacemaker

Core platform of cardiac rhythm management

Balloon angioplasty

Foundation of interventional cardiology

CREATE POWERFUL NEW CAPABILITIES 2

AVIM Therapy

Patented novel mechanism to treat hypertensive heart disease

Virtue SAB

Proprietary liquid infusion of extended-release SirolimusEFR™

REALIZE THROUGH COLLABORATION 3

Strategic partners

Development, commercialization and capital

Research partners

High-quality global pivotal trial execution

A Renaissance in Cardiac Pacing & Balloon Angioplasty

Renaissance (n): a Revival or Renewed Interest in Something; Learning from the Past to Create Something Better for the Future.

PACEMAKERS

Core platform of cardiac rhythm management



EST. 1958

- ~1.4M implants a year worldwide
- 65+ years as the definitive therapy for bradycardia & heart block

THE RENAISSANCE

- Conduction system pacing → standard of care
- Leadless pacing entering dual-chamber era, with single-device high-longevity approaches on the horizon

BALLOON ANGIOPLASTY

Foundation of interventional cardiology



EST. 1977

- Original PCI treatment and stent delivery platform
- Vessel prep for every PCI device: cutting, scoring, IVL

THE RENAISSANCE

- Drug-coated balloons lead “leave nothing behind”
- First US coronary DCB approved 2024
- DCB likely already >20% of PCI in EU, Japan, China

Procedure volumes and market figures are Company estimates; see corporate overview for sources.

1450 – 1600

THE RENAISSANCE

Rediscovery of Proven Foundations Sparks New Inventions

1600 – 1750

THE AGE OF ENLIGHTENMENT

Powerful New Capabilities Broaden & Strengthen Impact

Orchestra BioMed enters its Age of Enlightenment

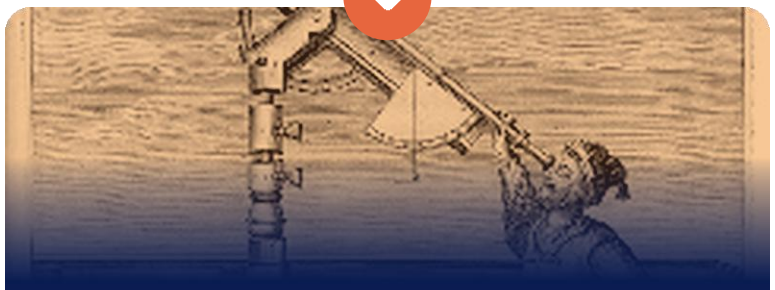
Renaissance Ideas Became Enlightenment Impact

Ideas Rediscovered in The Renaissance Were Turned, in The Enlightenment, into Tools and Institutions that Reached Far More People



SCIENCE

Copernicus places the sun at the center of the heavens (1543)



Galileo, Kepler, Newton: birth of physics & astronomy



KNOWLEDGE

Gutenberg's press (c. 1450); humanists recover classical texts

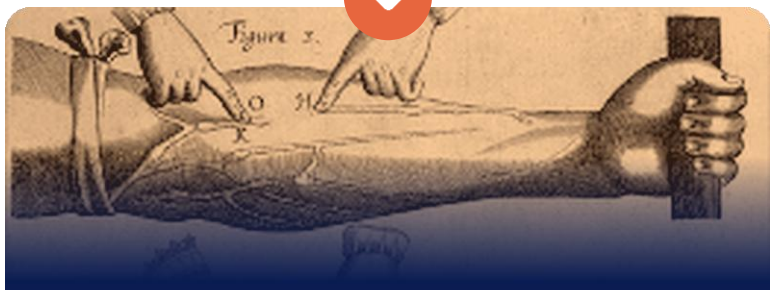


Scientific societies and journals; printed knowledge reaches a reading public



MEDICINE

Vesalius maps human anatomy from direct observation (1543)



Harvey demonstrates blood circulation; medicine built on experimental evidence

Our R&D Goal Is To Build On The Device Renaissance To Create An Enlightened Age Powered By **AVIM Therapy And Virtue SAB**

AVIM Therapy & Virtue SAB Enlighten the Device Renaissance



AVIM THERAPY

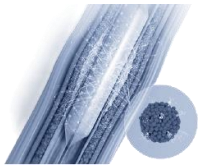
Atrioventricular Interval Modulation Therapy

ENLIGHTENMENT VISION

Cardiac pacing therapy that treats hypertensive heart disease

BROADER IMPACT POTENTIAL

Help address the #1 comorbidity in pacemaker-indicated patients and open pathway to treatment of new patients



VIRTUE SAB

Sirolimus AngioInfusion Balloon

ENLIGHTENMENT VISION

A better way to deliver proven sirolimus to help heal arteries post-intervention

BROADER IMPACT POTENTIAL

Enable superior drug delivery and extended release to drive better vessel healing and improved clinical outcomes

The Enlightenment Gave Birth to the Symphony Orchestra

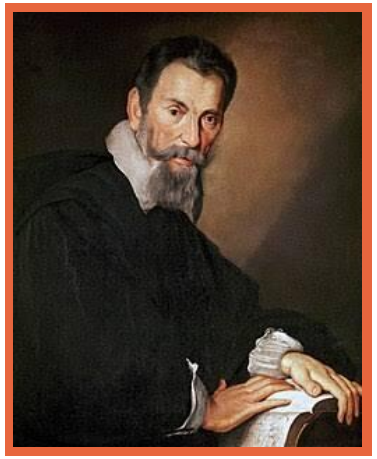
Driven by Innovation & Visionary Leadership

INSTRUMENTS
A blended, scalable sound

TRAINING
Disciplined, professional players

NOTATION
Music that travels abroad

ORCHESTRATION
The composer decides the sound

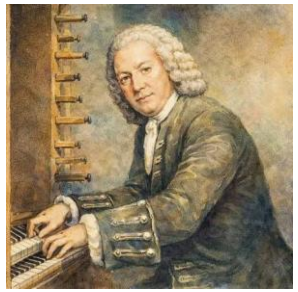


Claudio Monteverdi
(c.1600) –
The "Father" of the Symphony Orchestra



Antonio Vivaldi

Johann Sebastian Bach



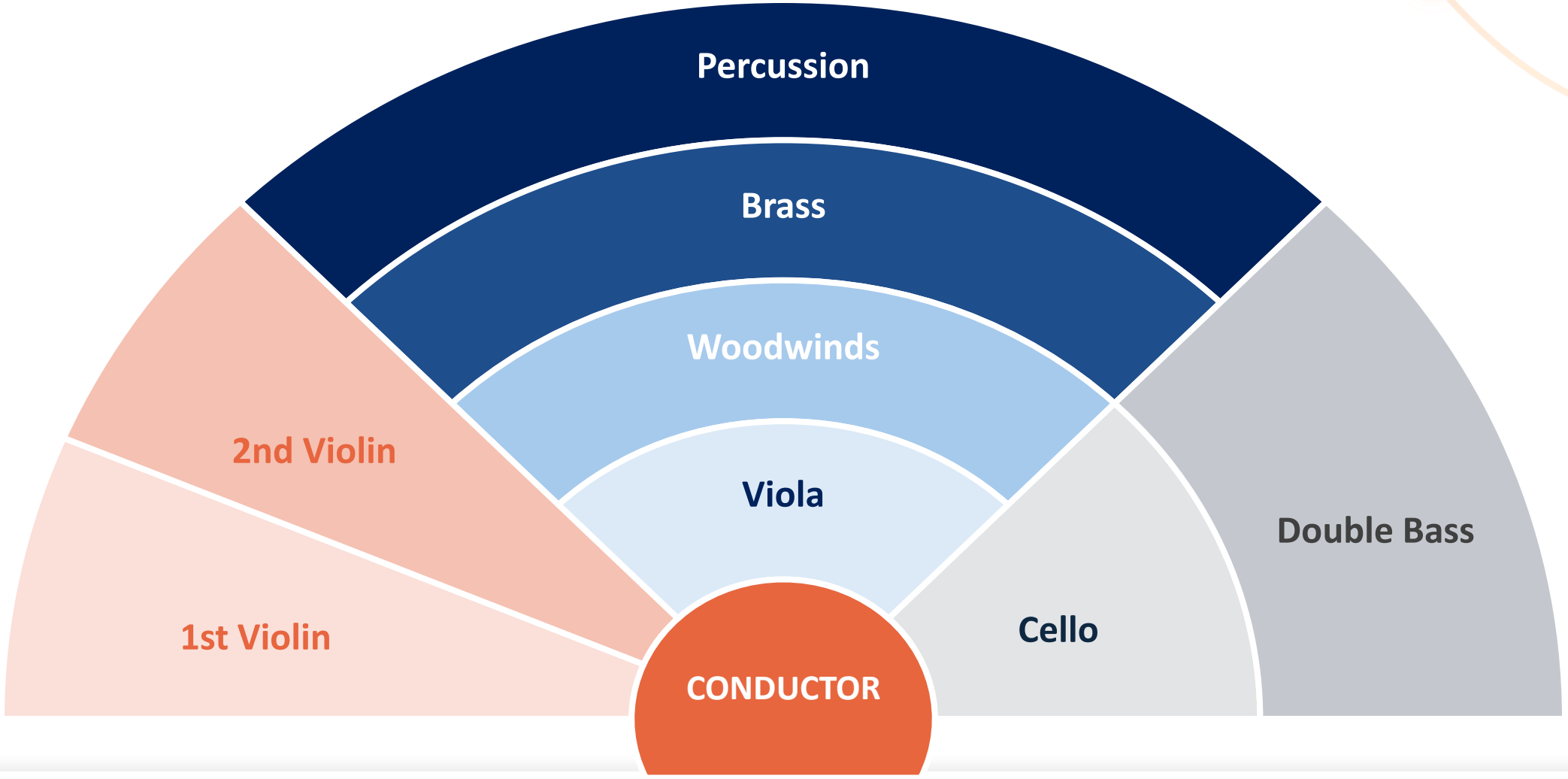
The Result: A More Powerful and Transportable Level of Performance and Artistry
Standard ensembles and printed scores let the same music be performed from Venice to London

An orchestra succeeds through extraordinary collaboration

> *"What more **miraculous creation of mankind** is there than the symphony orchestra — a hundred musicians **collaborating flawlessly** in the creation of a single sonority from moment to moment… We tend to take for granted the skill and sensitivity of such a **performing organism**, and we should take time to **marvel afresh that such a joint effort** is possible for human beings, so rich in communication, beauty and meaning."*
>
> **— KLAUS GEORGE ROY**

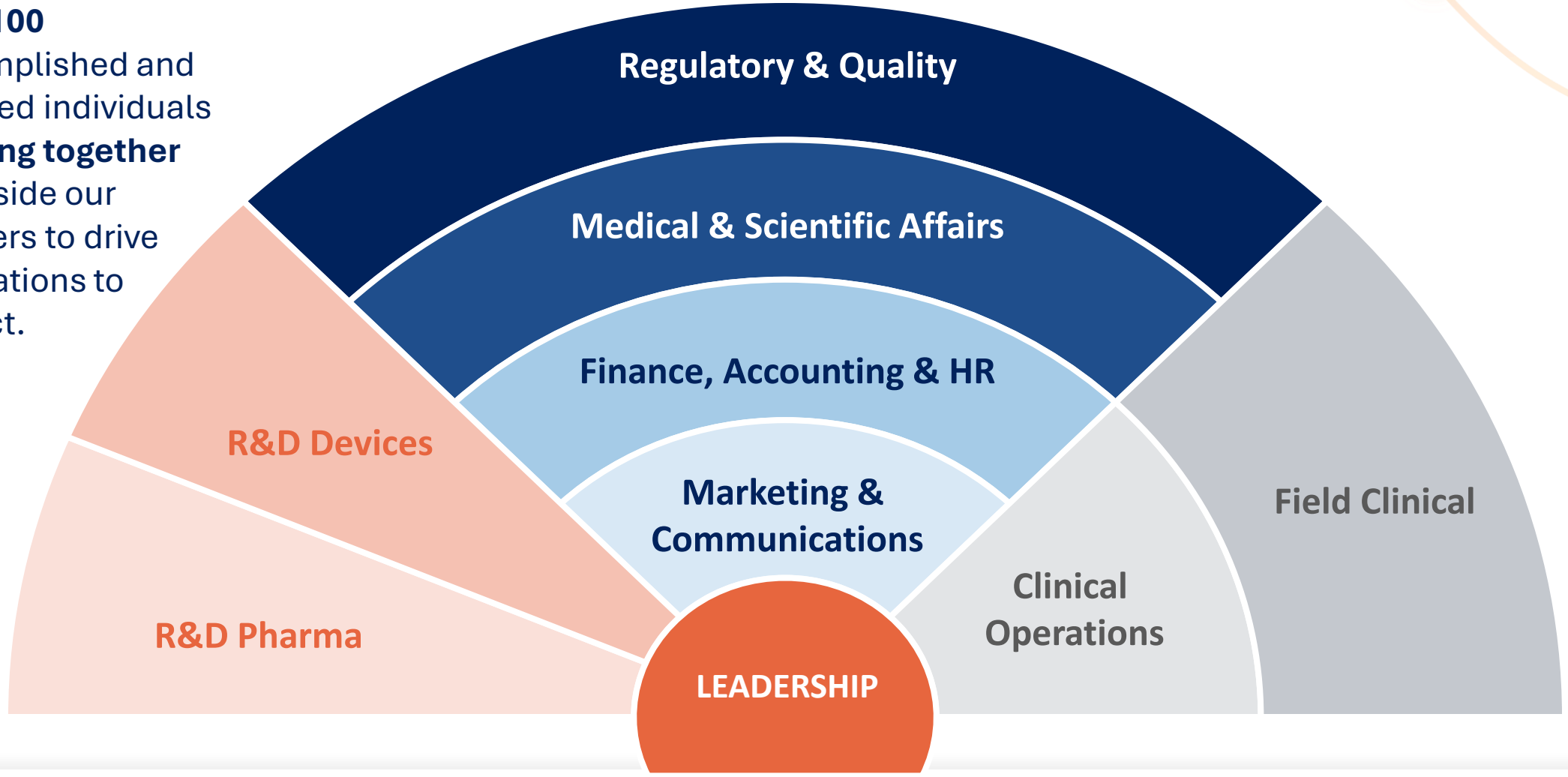
Orchestrating Innovation

The Symphony Orchestra



Orchestrating Innovation
Our Orchestra BioMed

Over **100** accomplished and talented individuals **working together** alongside our partners to drive innovations to impact.



Our Research Partners Include Physicians, Research Staff & **Patients**

BACKBEAT
GLOBAL PIVOTAL STUDY

- **349 patients** enrolled
- 92 sites
- 15 countries

Virtue Trial

- Enrolling 740 patients
- Up to 100 sites
- Expanding outside the U.S.

Our Partnership Model Optimizes Our Ability to Reach & Impact Patients Globally

WE FOCUS ON BEING GREAT AT:

- **High-impact innovation**
  differentiated technology with strong IP
- **Expert clinical execution**
  global pivotal trials that support regulatory approvals and optimized reimbursement
- **Value-creating partnerships**
  capital-efficient collaborations that create growth opportunities



WE RELY ON GREAT PARTNERS FOR:

- **Global commercialization**
  established sales, distribution, and support
- **Market leadership**
  trusted relationships, and deep field expertise
- **Operational & financial scale**
  proven manufacturing & strong balance sheets

We develop & prove novel therapies

We secure high-margin royalties without the cost structure

They commercialize at global scale

They secure significant revenue upside without R&D burden on their P&L

Virtue® Sirolimus AngioInfusion™ Balloon (SAB)

Darren R. Sherman · President & Chief Operating Officer

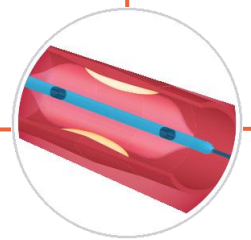
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Five Decades of Innovation in Interventional Cardiology

BALLOON ANGIOPLASTY

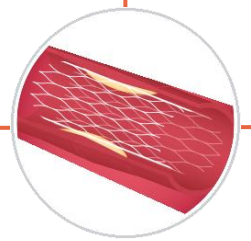
1977



- Opens the artery without surgery

BARE-METAL STENTS

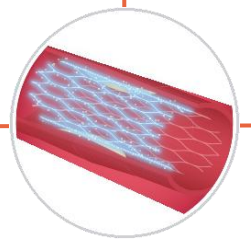
1994



- Solves recoil & abrupt closure
- Reduces restenosis ~30% vs balloon angioplasty[1,2]

DRUG-ELUTING STENTS

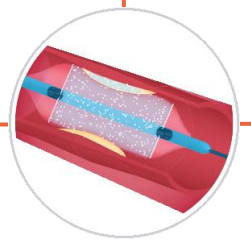
2003



- Further reduces restenosis[3]
- Limus improved outcomes vs paclitaxel[4]
- Leaving a stent behind carries **long-term TLF risk of ≈ 3% annually[5]**

DRUG-COATED BALLOONS

2024



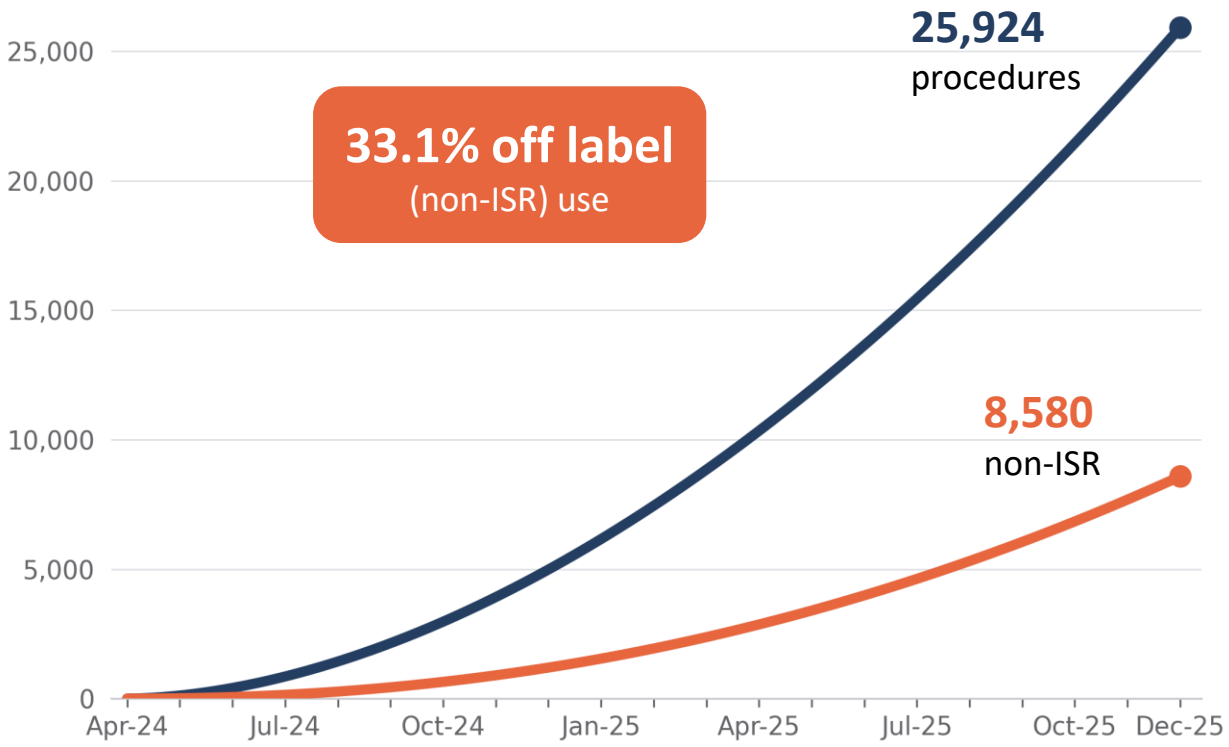
- Treats ISR without another stent layer
- **AGENT paclitaxel DCB 32.7% TLF at 3 Years[6]**
- No reported abrupt closures in trials

Opportunity Remains to Optimize Outcomes

[1]Serruys et al. N Engl J Med 1994;331:489 (BENESTENT). [2]Fischman et al. N Engl J Med 1994;331:496 (STRESS). [3]Moses et al. N Engl J Med 2003;349:1315 (SIRIUS). [4]Zhang et al. PLOS ONE 2014;9:e97934. [5]von Birgelen et al. J Am Coll Cardiol 2012;59:1350. [6]Yeh et al. JAMA 2024;331:1015; AGENT IDE 3-yr, CRT 2026. AGENT™ is a trademark of Boston Scientific Corporation.

US DCB Adoption With 1/3 Off Label Use Reflects Clinical Need

NCDR CathPCI Registry, Cumulative US DCB Procedures[1]



~50%

of TCT PCI talks were on DCB*

"2 years in a row now DCB trials are really making an impact in the US

Kirtane, MD · TCT 2026

"Uptake has been rapid … one-year target vessel outcomes were reassuring for both ISR and non-ISR lesions

Lalani, MD · CathPCI Registry, TCT 2026

DCB Momentum Is Strong And Growing, Virtue ISR Trial Randomized 1:1 vs AGENT DCB

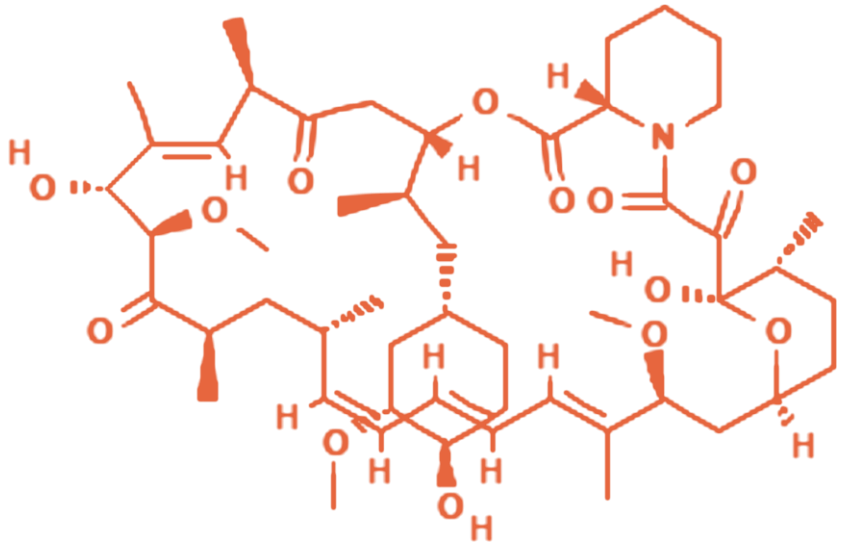
[1]Adapted from Lalani, TCT 2026; Lalani et al. Circ Cardiovasc Interv 2026;19:e016625. April 2024 to December 2025. *Orchestra BioMed analysis of the TCT 2026 coronary program.

Leveraging the Familiar



BALLOON ANGIOPLASTY

Utilized in coronary interventions since Gruentzig's 1st angioplasty in 1977[1]



SIROLIMUS

Used clinically since 1993[2], proven superior to paclitaxel in large DES meta-analysis, but challenging for DCB delivery[3]

Proven Procedure and Drug

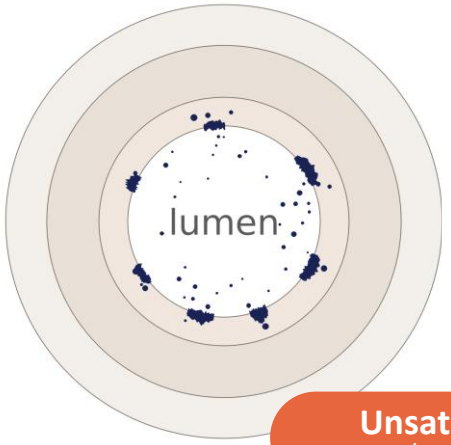
[1]Gruentzig. Lancet 1978;1:263. [2]Murgia et al. Kidney Int 1996;49:209. [3]Zhang et al. PLOS ONE 2014;9:e97934.

Evolution of Coronary Drug Delivery

From Surface Coatings To Transmural Delivery

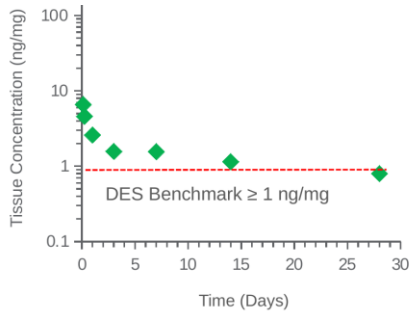
COATINGS FOR DRUG DELIVERY

Via Polymer on DES & Coating on Balloon



XIENCE™ V

Everolimus-eluting Coronary Stent



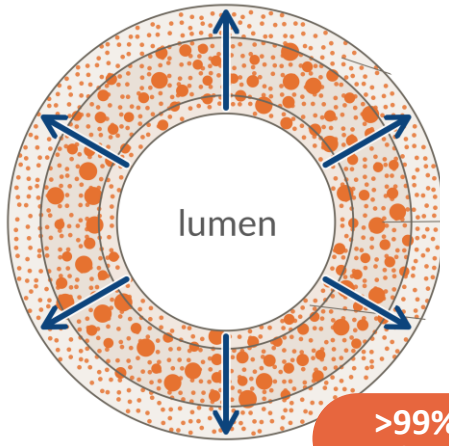
Unsaturated
~1 ng/mg at 30 days

Limitations of Coatings

Dose is limited · Drug is lost in transit · Transfer is uneven

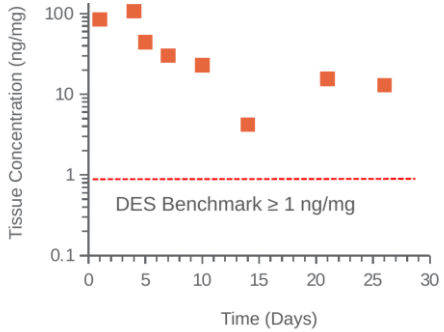
LIQUID DRUG INFUSION

Transmural SirolimusEFR™ Particle Infusion



Virtue® SAB

Sirolimus AngioInfusion™ Balloon

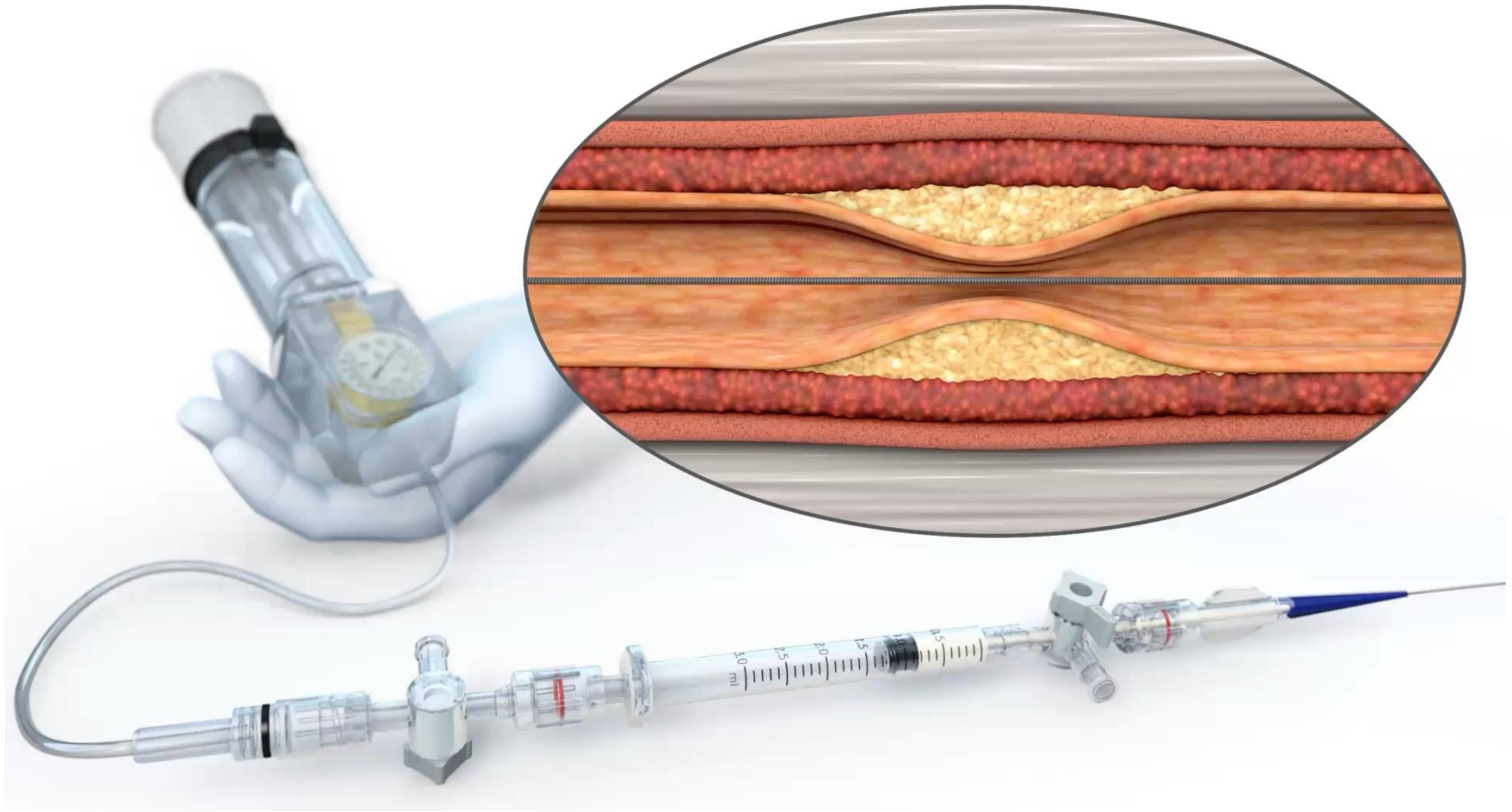


>99% Saturated
13 ng/mg at 30 days

Designed to saturate binding sites, to optimize inhibition of cell proliferation & modulate inflammation through the critical healing period

Brodmann, EuroPCR 2015. Tzafriri et al. Biomaterials 2020;260:120337. Tzafriri et al. J Control Release 2019;310:94. Kolachalama et al. Circ Cardiovasc Interv 2013;6:415. Virtue SAB Mechanism 0010 on file. PK adapted from Granada et al. EuroIntervention 2016;12:740 and Perkins et al. J Interv Cardiol 2009;22(Suppl 1):S28. XIENCE V is a trademark of the Abbott Group of Companies

Virtue® SAB Liquid Drug Infusion



Core Pharmaceutical Technology: SirolimusEFR™

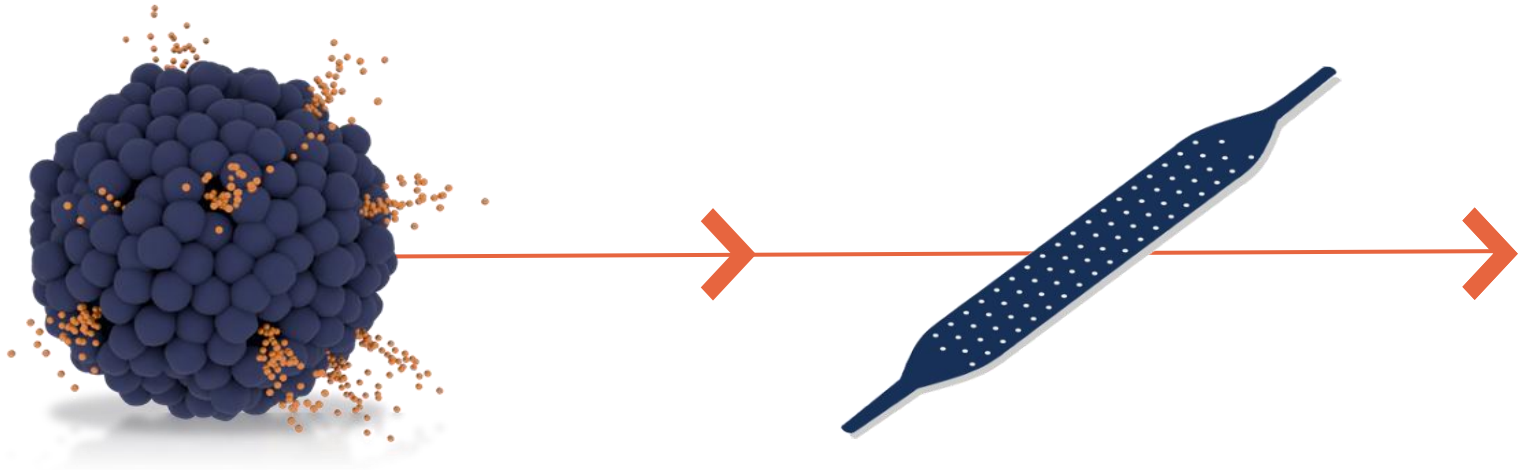
A first-of-its-kind extended-release sirolimus

- Sustained release
- Inhibiting cell proliferation & modulating inflammation

AngioInfusion™ Balloon

1st

in a potential series of application-specific delivery devices



Potential future applications where sirolimus has established utility or approved indication

- Cardiovascular*
- Immune / Transplant
- Renal / Urologic
- Pulmonary
- Skin / Integumentary
- GI / Hepatic
- Endocrine / Metabolic
- Nervous System
- Oncology
- Reproductive

*Current device application shown here; broader rapamycin product potential may extend beyond cardiovascular use

The Virtue ISR Coronary Pivotal Trial

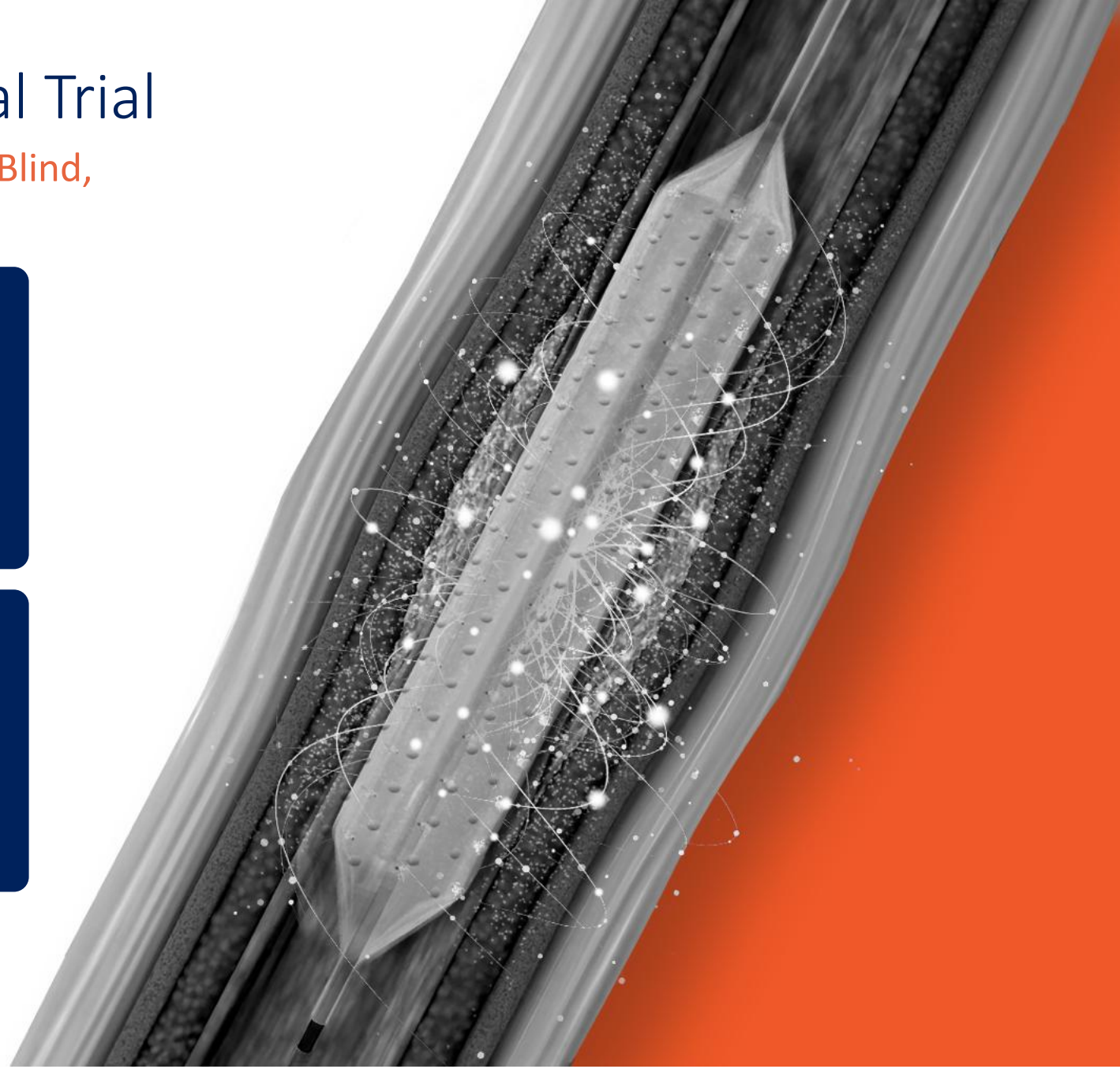
Randomized, Prospective, Multi-Center, Single-Blind, Non-Inferiority Trial vs AGENT™ DCB

740 Patients
with ISR lesions

Up to 100 Sites
Global

1:1 Randomized
Virtue® SAB vs AGENT™ DCB

12-Mo TLF
Primary endpoint; superiority test upon non-inferiority



CONTEMPORARY DESIGN, IMPROVING ON SABRE

Includes ≤ 30% residual stenosis, standard of care lesion preparation & intravascular imaging

Virtue ISR Trial Clinical Investigation Protocol 0072. NCT07045194. AGENT™ is a trademark of Boston Scientific Corporation.

Today's Presenters & Co-Principal Investigators



DUANE S. PINTO, MD, MPH

Senior Clinical Advisor (Orchestra), Chief Medical Officer, JenaValve Technologies, Associated Professor of Medicine, Harvard Medical School

- Graduated *cum laude* from Dartmouth College with a degree in Biological Sciences before earning his medical degree from Georgetown University
- Completed his medical training and cardiology fellowships at Beth Israel Deaconess Medical Center and is an Associate Professor of Medicine at Harvard Medical School
- Nationally recognized interventional cardiologist, he specializes in complex coronary, peripheral vascular, and structural heart procedures
- Held leadership positions at Beth Israel Deaconess Medical Center, including Chief of Interventional Cardiology and Cardiology Fellowship Director



ALLEN JEREMIAS, MD, MSc

Director, Cardiac Catheterization Laboratory, St. Francis Hospital & Heart Center, NY
Executive Director, OPCI

- Medical training at The Cleveland Clinic Foundation, Stanford University School of Medicine and Harvard Medical School
- High-volume interventional cardiologist since 2006, specializing in complex coronary intervention and CTO procedures
- Considered one of the foremost authorities in coronary physiology and intravascular imaging to optimize coronary interventions
- Global principal investigator of several major clinical trials, including DEFINE PCI, ALL RISE, Virtue ISR and DEFINE GPS — a landmark randomized trial of coronary physiology for PCI guidance
- Recognized as a top doctor by Castle Connolly
- Elected by SCAI, CRF and ACC as a leading interventional cardiologist

Virtue® Sirolimus AngioInfusion™ Balloon (SAB)

Allen Jeremias, MD
St. Francis Hospital, Roslyn, NY

Virtue Trial

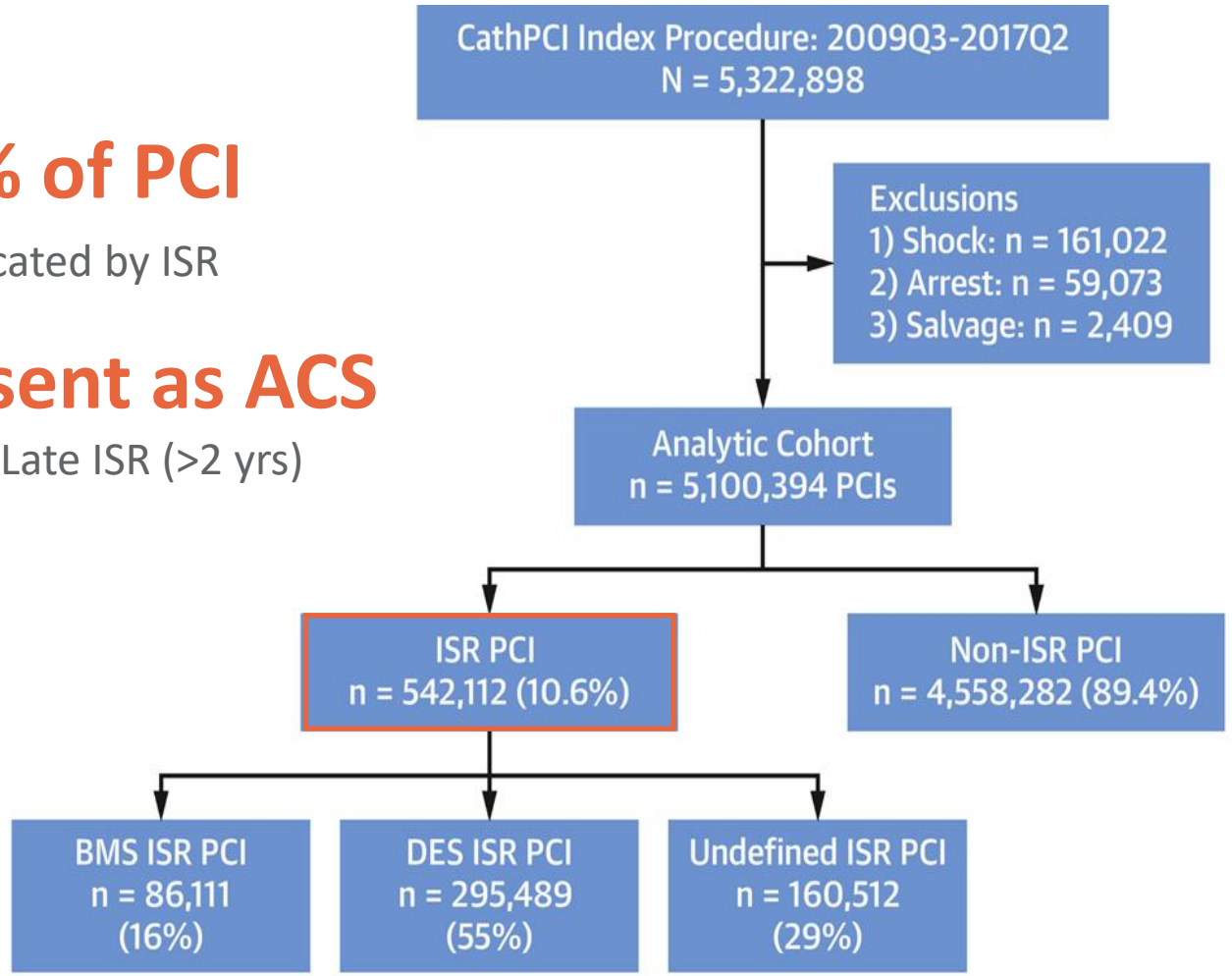
Coronary In-Stent Restenosis Remains a Significant Challenge

10.6% of PCI

complicated by ISR

79% Present as ACS

Half is Very Late ISR (>2 yrs)



Adapted from Moussa et al. J Am Coll Cardiol 2020;76:1521.

NCDR Cath PCI	ISR PCI (n = 542,112)
CAD presentation	
No angina	4.2
Symptom unlikely to be ischemic	1.7
Stable angina	15.1
Unstable angina	51.8
NSTEMI	18.7
STEMI	8.5
ISR time frame	
<1 month	2.2
1-5 months	10.0
6-12 months	12.8
1-2 yrs	14.8
>2 yrs	50.4
Unknown	9.8

Late ISR is predominantly biological, not mechanical failure[2]

[1]Moussa et al. J Am Coll Cardiol 2020;76:1521. [2]Shlofmitz et al. Circ Cardiovasc Interv 2019;12:e007023. ***Definitions:*** Acute coronary syndrome = unstable angina (UA), NSTEMI, STEMI; PCI (Percutaneous Coronary Intervention), In-Stent Restenosis (ISR), DES (Drug-eluting Stent)

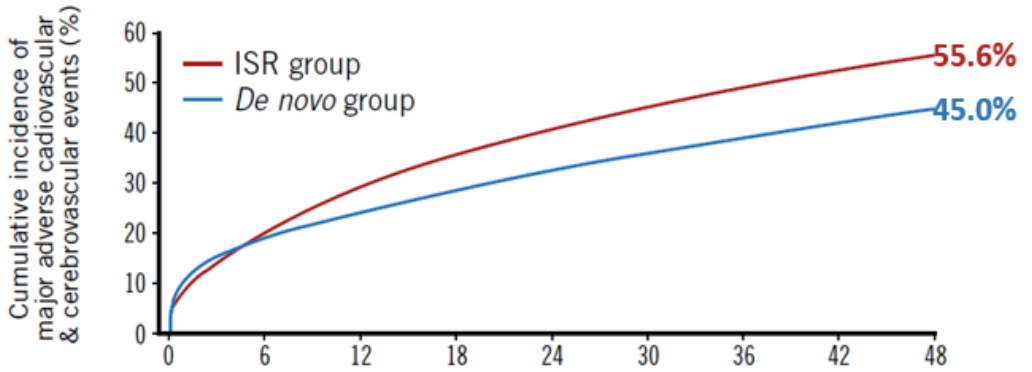
Limitations of Treating ISR with Another Layer of Drug-Eluting Stents

More Metal Associated with Worse Outcomes Driving the Pursuit of Drug-Coated Balloons

ADDITIONAL LAYERS OF DES

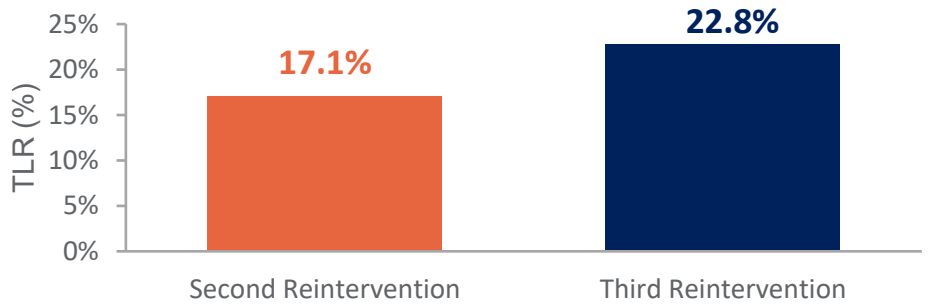
- Are associated with significantly worse outcomes[1]
- Increase stent fracture and thrombosis
- Compromise lumen in small vessels
- Require long-term DAPT, associated with bleeding & mortality[2,3]
- Limit future treatment options

24% HIGHER RISK OF MACCE WITH ISR[1]



ACC/NCDR CMS Database 4-Year Outcomes[1]

HIGHER TLR WITH EACH ADDITIONAL STENT[4]



Adapted from Tamez et al.[1] and Kastrati et al.[4]

[1]Tamez et al. EuroIntervention 2021;17:e380. [2]Richardt et al. JACC Cardiovasc Interv 2013;6:905. [3]Campo et al. J Am Coll Cardiol 2014;63:506; Valgimigli et al. Circulation 2012;125:2015. [4]Kastrati & Cassese. J Am Coll Cardiol 2020;76:1532. ***Definitions:*** DCB (Drug-Coated Balloon), In-Stent Restenosis (ISR), DES (Drug-eluting Stent), Dual Antiplatelet Therapy (DAPT), MACCE (Major Adverse Cardiovascular & Cerebrovascular Events: death from any cause, MI, stroke, & repeat revascularization), Target Lesion Revascularization (TLR)

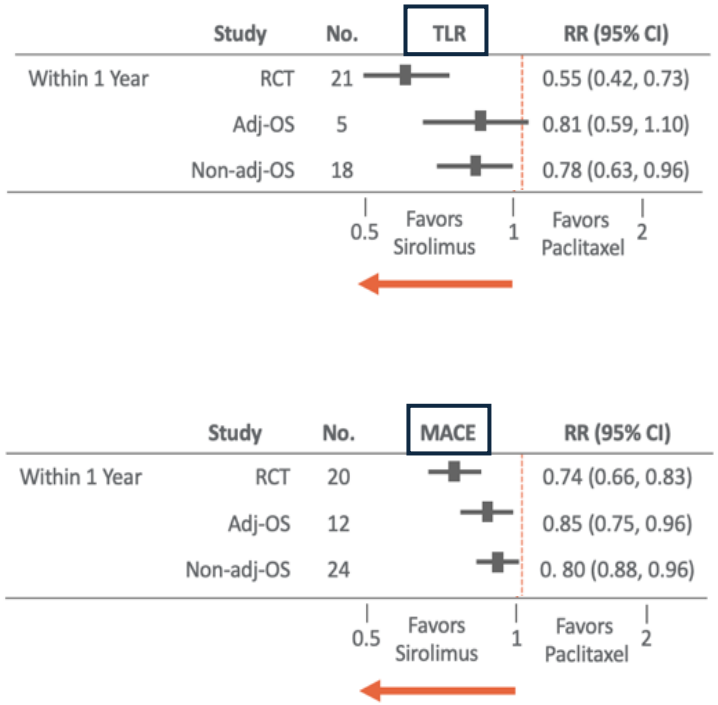
The Data Confirm that Sirolimus is Optimal

Limus-Eluting Stents Demonstrated Superior Safety & Efficacy vs. Paclitaxel

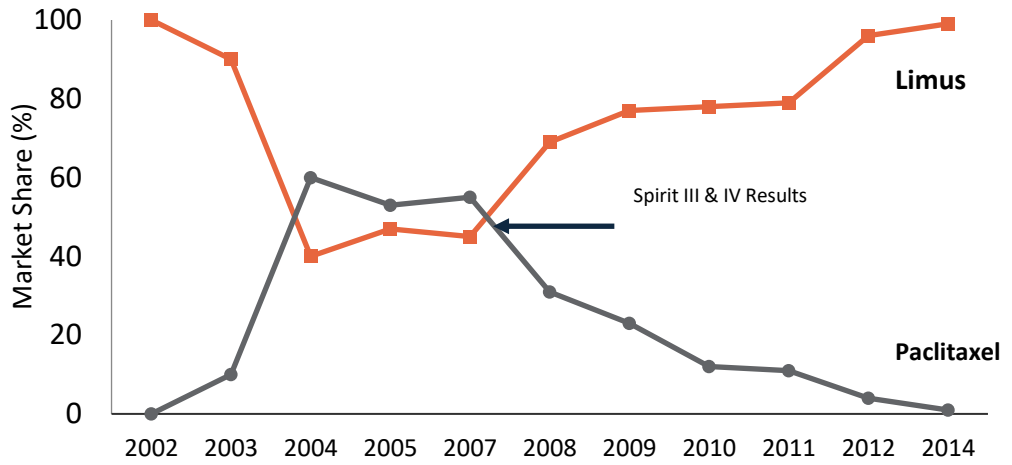
In meta-analysis of 76 studies including 26 RCT **limus stents** showed[1]

45%
Lower Risk of TLR

26%
Lower Risk of MACE



Paclitaxel No longer in Coronary DES



Limus Improved Outcomes, But Leaving A Stent Behind Carries Long-term TLF Risk of ≈ 3% Annually[2]

[1]Zhang et al. PLOS ONE 2014;9:e97934. Meta-analysis of 76 studies including more than 15,000 patients in RCTs and over 70,000 patients in adjusted observational studies. [2]von Birgelen et al. J Am Coll Cardiol 2012;59:1350. ***Definitions:*** Randomized Controlled Trial (RCT), Target Lesion Revascularization (TLR), Major Adverse Cardiac Events (MACE), Drug-Eluting Stent (DES)

Sirolimus is Optimal and Challenging for Balloon-Based Delivery[1]

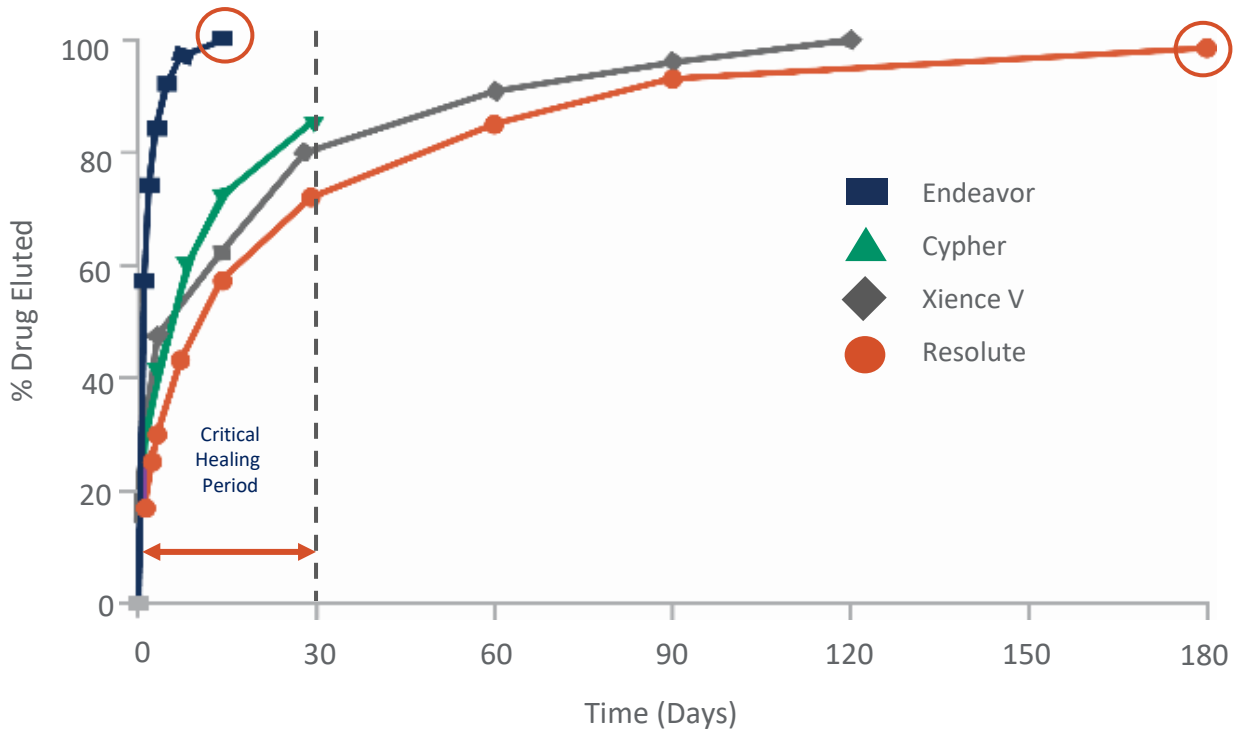
	SIROLIMUS	PACLITAXEL
Mode of Action	**Cytostatic** Does not kill the cell	**Cytotoxic** Leads to cell death
Mechanism	Binds to FKBP12 to inhibit mTOR, **arresting SMC proliferation & modulating inflammation**	Binds to stabilize microtubules, arresting SMC proliferation & inducing apoptosis
Therapeutic Window	**Broad** Wide margin between effective dose & toxicity	**Narrow** Slight change in dose may impact safety & efficacy
Tissue Uptake	**Slow and limited distribution**	**Fast**
Tissue Retention	**Short**	**Long**

Clinical Outcomes Depend On Adequate Sirolimus Tissue Concentrations Through The Critical Healing Period

[1]Habib & Finn. Interv Cardiol Clin 2016;5:321. ***Definitions:*** smooth muscle cell (SMC)

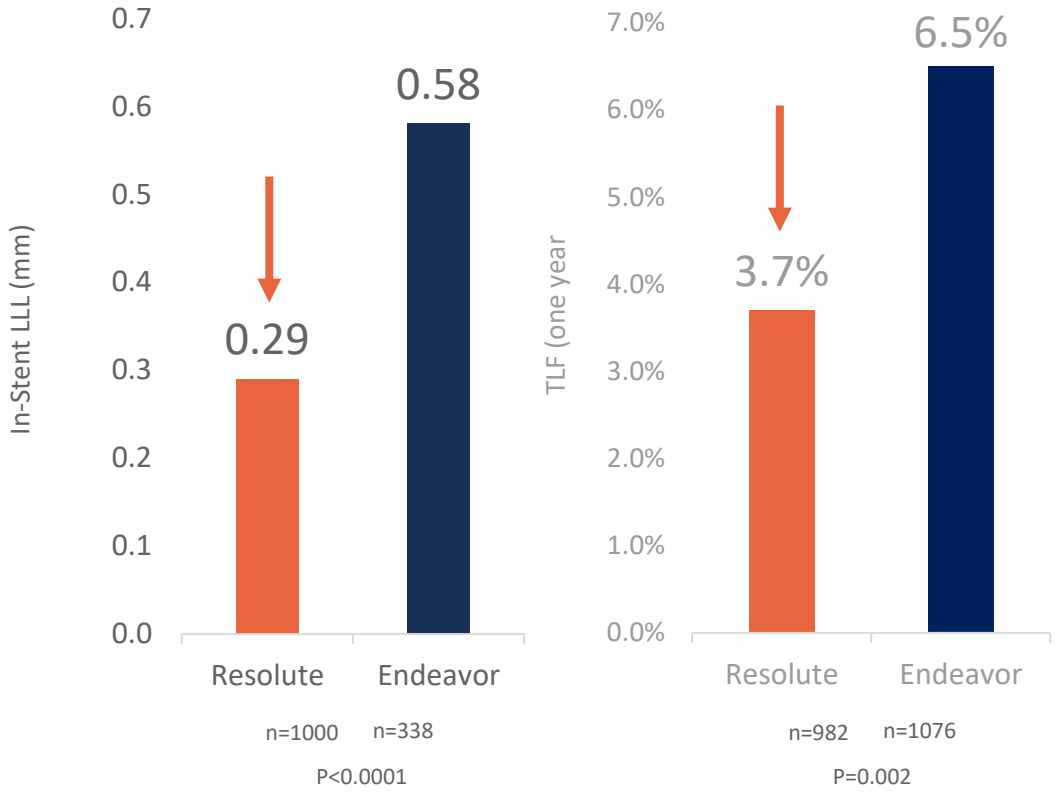
Sustained Limus Dose Improved Outcomes

Endeavor Fails to Elute Through Critical Healing Period[1]



Endeavor **Phosphorylcholine** (PC) polymer
Resolute **BioLinx** Tri-polymer blend

Resolute Demonstrates Lower LLL & TLF than Endeavor[2,3]



[1]https://slideplayer.com/slide/5787004; [2]Tada et al. Am Heart J 2013;165:80. [3]Leon, LBT III, Session 3014, ACC 2011. ***Definitions***: TLF (Target Lesion Failure)

Coatings For Drug Delivery Have Limitations

Optimal Outcomes Depend on Sustained Delivery of an Adequate Dose

DRUG DOSE LIMITED

by balloon surface area & coating integrity



~ 1 - 4 ug/mm²

nominal dose[1,2]

DRUG LOST IN TRANSIT

requiring rapid navigation, risking emboli & reducing delivered dose

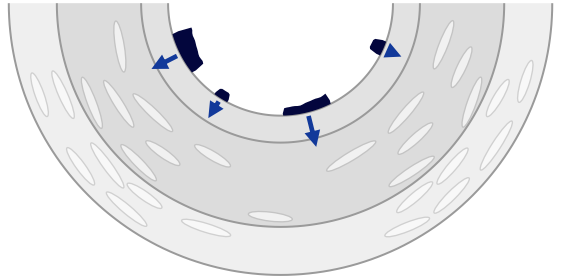


Up to ~80%

lost in transit[3]

TRANSFER IS UNEVEN

with variable contact & drug diffusion from the surface[4-6]

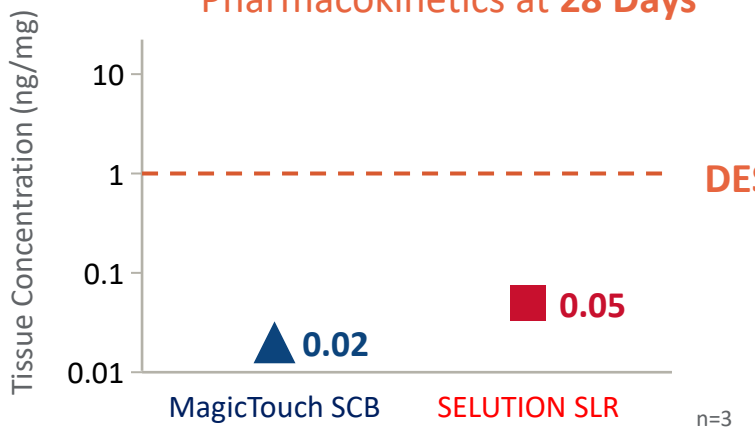


[1]Jeger et al. JACC Cardiovasc Interv 2020;13:1391. [2]MagicTouch dose per Ninomiya et al. JACC Cardiovasc Interv 2023;16:2884. [3]Brodmann, EuroPCR 2015. [4]Tzafriri et al. Biomaterials 2020;260:120337. [5]Tzafriri et al. J Control Release 2019;310:94. [6]Kolachalama et al. Circ Cardiovasc Interv 2013;6:415.

Optimal Outcomes Depend on Sufficient and Sustained Sirolimus

Inadequate Tissue Concentrations

Sirolimus Coated Balloons
Pharmacokinetics at **28 Days**



Adapted from Kawai et al[1]

SCBs face challenges achieving & maintaining adequate tissue concentrations through the critical healing period

Opportunity Remains to Optimize Sirolimus Delivery

SELUTION4ISR RCT
Primary Endpoint at 1 Year[2]

	SELUTION SLR	SOC ~80% DES/20% BA
TLF %	**16.2**	**14.5**

n=390

Non-inferior to SOC

Per Protocol SELUTION SLR did not meet noninferiority vs DES for single-layer ISR (14.2% vs 6.5% TLF)

[1]Kawai et al. Catheter Cardiovasc Interv 2025;105:1434. [2]Cutlip et al. J Am Coll Cardiol 2026; doi:10.1016/j.jacc.2026.03.021. SELUTION SLR is a trademark of M.A. Med Alliance SA. M.A. Med Alliance SA is a Cordis company. ***Definitions***: (SCB) sirolimus coated balloons, (DES) drug-eluting Stents, (BA) balloon angioplasty

Virtue® SAB: A Fundamentally Different Approach

Designed to Optimize Sirolimus Delivery

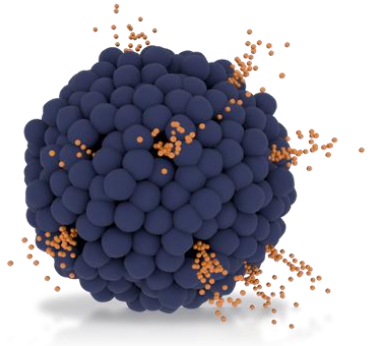
Protected **large liquid volume infusion** for immediate transmural distribution of **SirolimusEFR**[1,2]

Sustained transmural sirolimus release through the critical healing period[2-5]

Designed to saturate binding sites in the vessel wall to maximize inhibition & modulate inflammation[2-5]

Eliminated prior to degradation, avoiding inflammation associated with polymer degradation

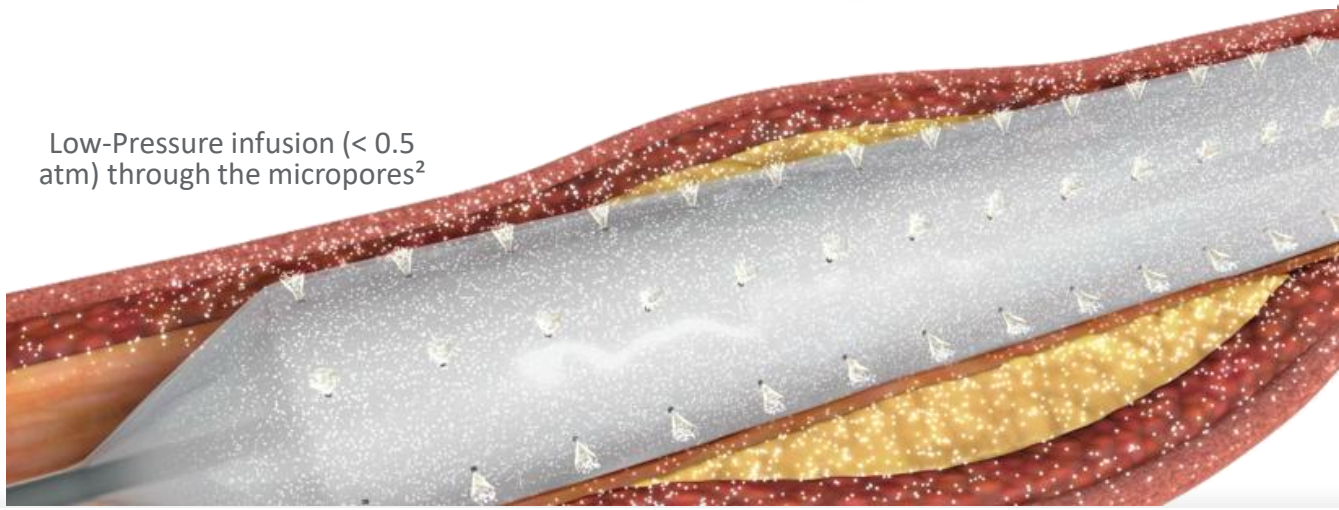
SirolimusEFR™
Submicron Encapsulated Particle



AngioInfusion™ Balloon
Non-Coated, Microporous



Low-Pressure infusion (< 0.5 atm) through the micropores[2]



[1]IFU. [2]Virtue SAB Mechanism 0010 on file. [3]Granada et al. EuroIntervention 2016;12:740. [4]Tzafriri et al. J Control Release 2012;161:918. [5]Levin et al. PNAS 2004;101:9463. ***Definitions:*** Immediate defined as during balloon inflation

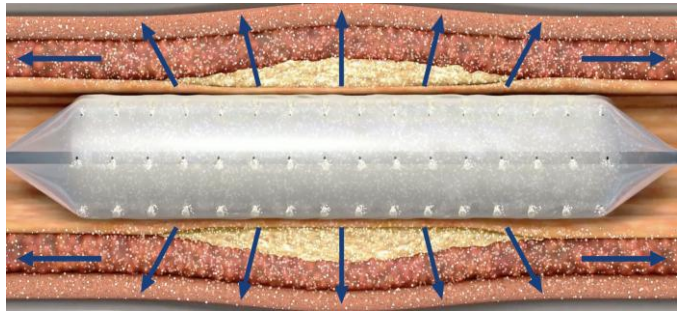
Virtue SAB Mechanism of Action

Saturated and Sustained Transmural Release[1]

LARGE LIQUID VOLUME INFUSION
of SirolimusEFR

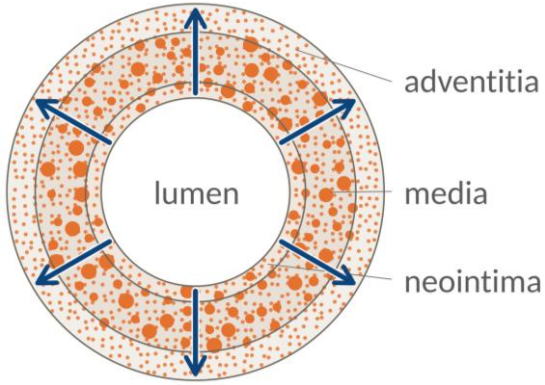
- **> 10X** more liquid than space available in the vessel wall[1,2]
- **> 2.5X** larger dose than DCB & DES[1,3]

Radial, circumferential & longitudinal



IMMEDIATE TRANSMURAL DISTRIBUTION
of a variable-sized array of submicron SirolimusEFR[2,5,6]

- Smaller particles **reach deep** into the media & adventitia
- Larger particles distribute within the layers **around & along the vessel**

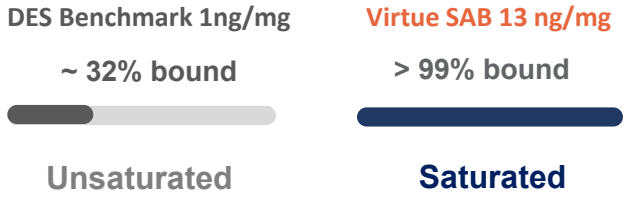


PARTICLES SUSTAIN TRANSMURAL RELEASE
saturating binding sites to maximize inhibition & modulate inflammation[2,4-6]

- Extended release through the critical healing period

Sirolimus Inhibits Where Bound

Tissue Concentrations at ~30 Days



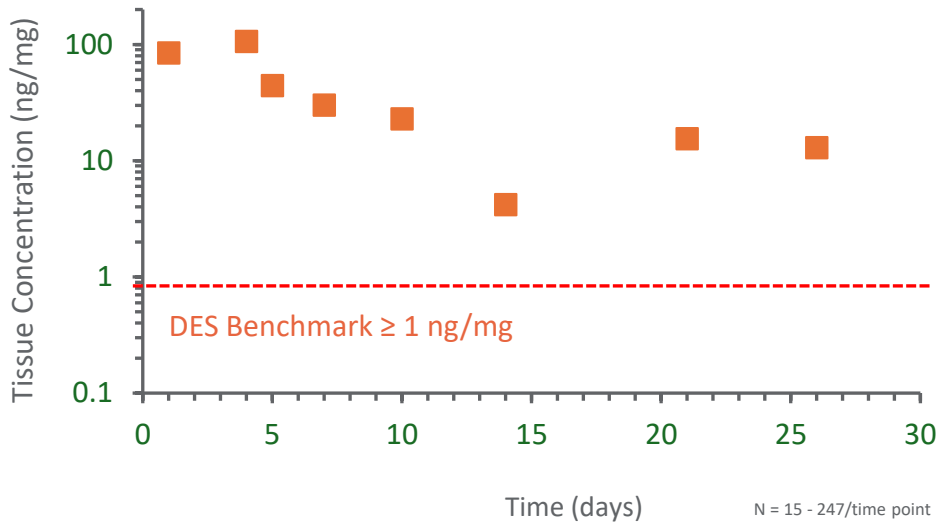
In Contrast, Drug-coated Balloons Deliver Lower Doses, Not Enough To Saturate Through The Healing Period

[1]IFU. [2]Virtue SAB Mechanism 0010 on file. [3]Wijayanto et al. J Saudi Heart Assoc 2026;38:17. [4]Granada et al. EuroIntervention 2016;12:740. [5]Tzafriri et al. J Control Release 2012;161:918. [6]Levin et al. PNAS 2004;101:9463. ***Definitions:*** Immediate defined as during balloon inflation

Virtue® SAB Exceeds Published Tissue Concentrations of Proven DES

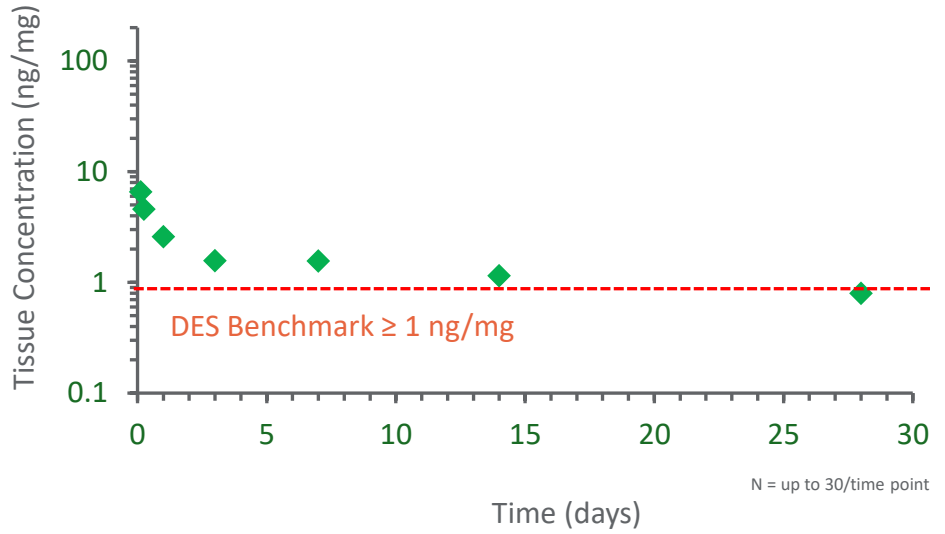
Through the Critical Healing Period

Virtue SAB



Adapted from Granada et al. EuroIntervention 2016;12:740

Xience™ V Everolimus-eluting Coronary Stent[1]



Adapted from Perkins et al. J Interv Cardiol 2009;22(Suppl 1):S28

[1]XIENCE V is a trademark of the Abbott Group of Companies

SABRE Design

Virtue SAB Pilot Trial

Design
Prospective, multicenter study evaluating Virtue® SAB in patients with coronary ISR

Number of Subjects
50

Primary Safety Endpoint
30-day TLF
- cardiac death
- target vessel MI
- clinically driven TLR

Primary Efficacy Endpoint
In-stent LLL at 6 months by QCA
Independent core lab adjudication

Follow-Up
30 days, 6 months, 1 year, 2 years & 3 years

Independent Core Lab / DSMB
Cardiovascular Research Foundation (CRF)



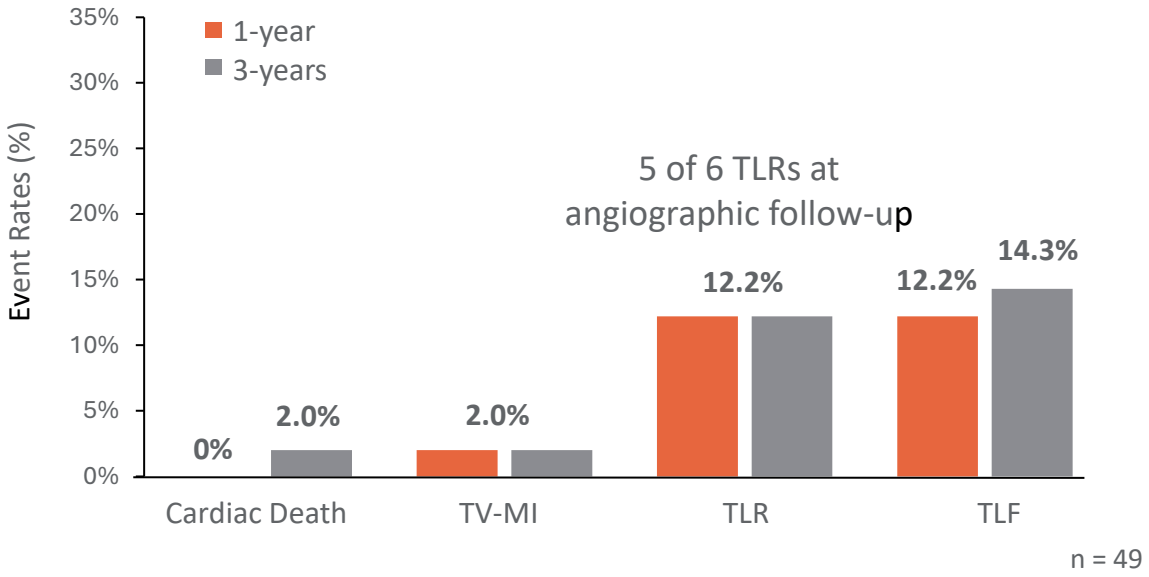
- Principal investigator – Stefan Verheye, M.D., Ph.D.
- 9 Sites, 4 countries

Verheye et al. JACC Cardiovasc Interv 2017;10:2029. ***Definitions***: TLF (Target Lesion Failure), TLR (Target Lesion Revascularization) LLL (Late Lumen Loss), MI (Myocardial Infarction).

SABRE Trial 3-Year Results

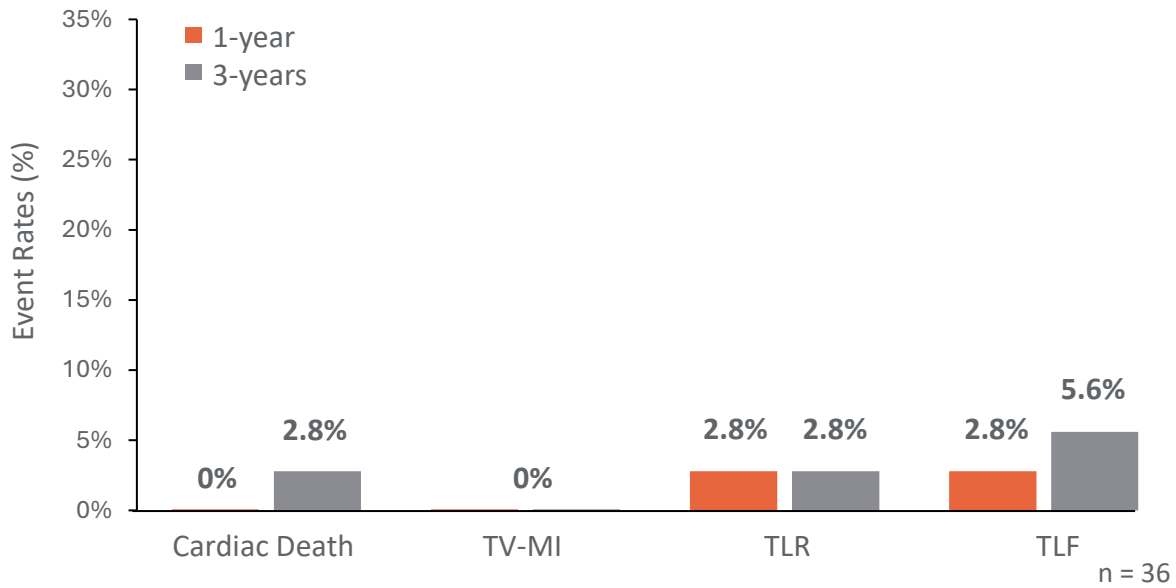
Prospective, Multi-Center, Single-Arm, Coronary ISR Trial

Intention-to-Treat



- **14.3% TLF at 3 years**
- No additional TLR from 1–3 years

Per-Protocol



- **5.6% TLF at 3 years**
- No additional TLR from 1–3 years

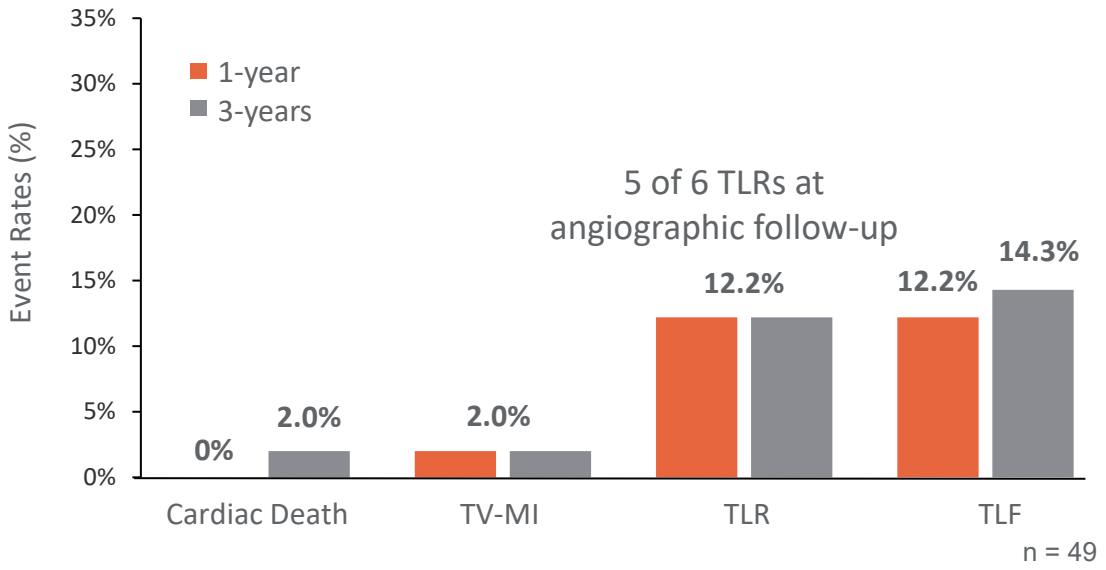
Low Event Rates Despite Including ≤ 40% Residual Stenosis & Mandatory 6-month Angiographic Follow-up

[1]Verheye et al. JACC Cardiovasc Interv 2017;10:2029. [2]Granada, SABRE 3-yr, TCT 2018. Per-protocol: revised analysis set meets the criteria of the In-Stent Restenosis IDE study population. ***Definitions:*** Target lesion revascularization (TLR), Target lesion failure (TLF), Target vessel myocardial infarction (TV-MI)

3-Year ITT Outcomes in Coronary ISR

Virtue SAB Event Rates to 3 Years

SABRE Prospective, Multi-Center Trial[1,2]

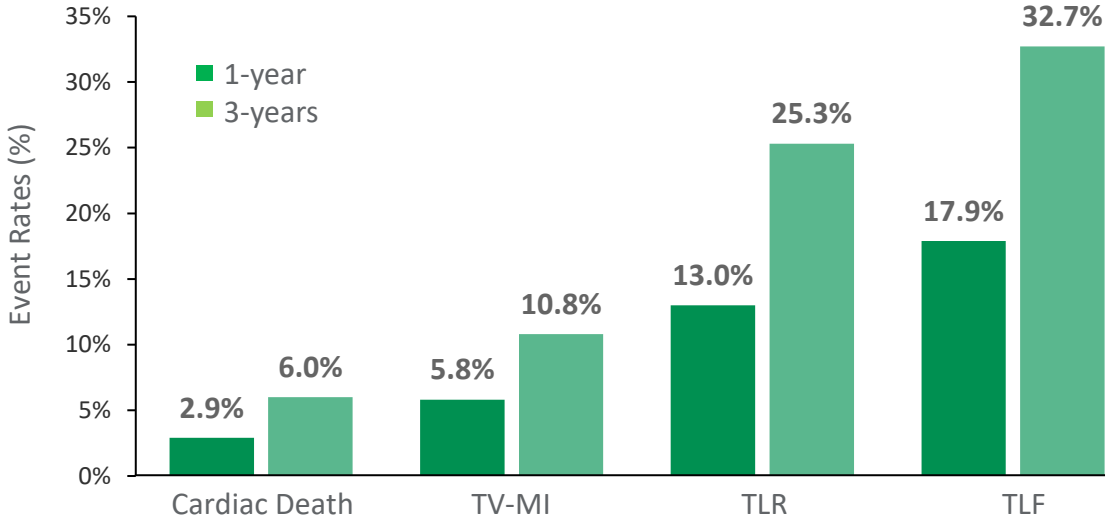


n = 49

- **14.3% TLF at 3 years**
- No additional TLR from 1–3 years
- Included ≤ 40% residual stenosis & angiographic follow-up

AGENT DCB Event Rates to 3 Years

Boston Scientific's Randomized IDE Trial[3,4]



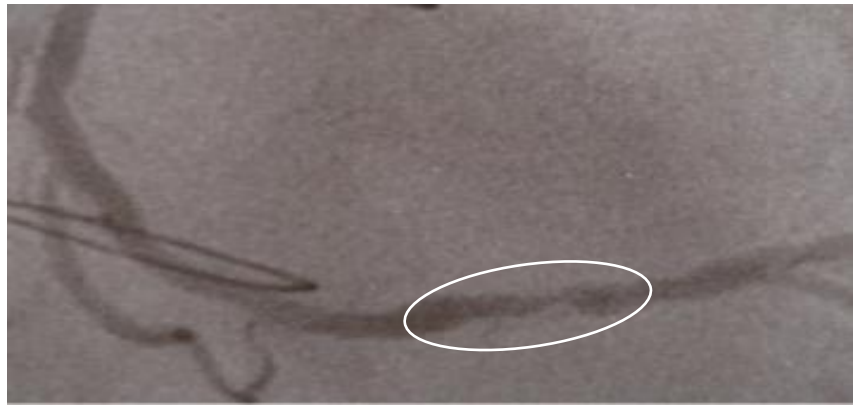
n = 406

- **32.7% TLF at 3 years**
- Included < 30% residual stenosis
- Intravascular imaging & advanced lesion preparation

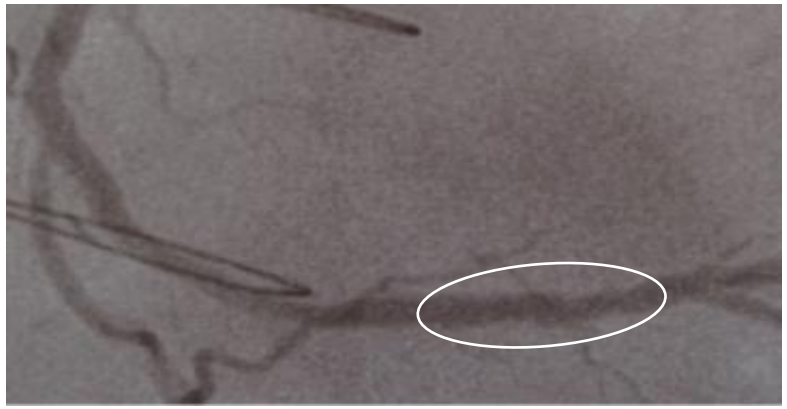
Separate Trials With Differing Designs; No Head-to-head Comparison

[1]Verheye et al. JACC Cardiovasc Interv 2017;10:2029. [2]Granada, SABRE 3-yr, TCT 2018. [3]Yeh et al. JAMA 2024;331:1015. [4]AGENT IDE 3-yr, CRT 2026. ***Definitions:*** Target lesion revascularization (TLR), Target lesion failure (TLF), Target vessel myocardial infarction (TV-MI)

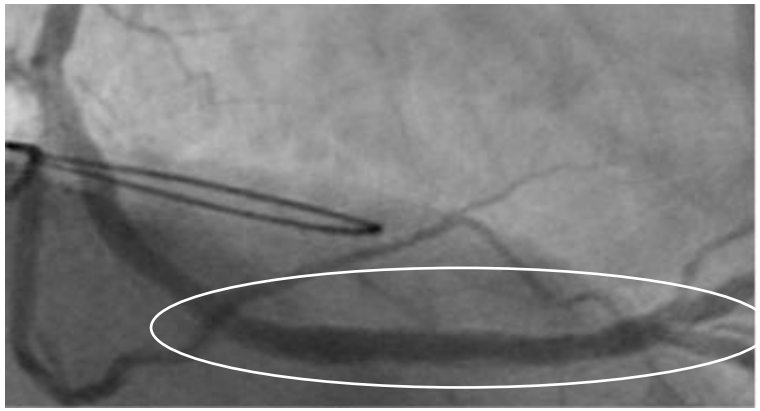
SABRE Trial Case 10-01



10-01 **Baseline**



Post Virtue SAB 2.75 x 15 mm

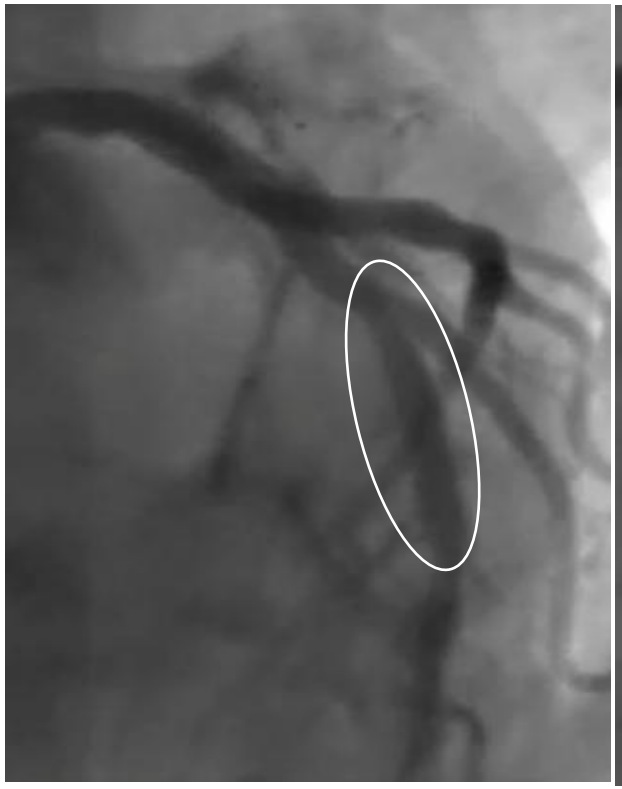


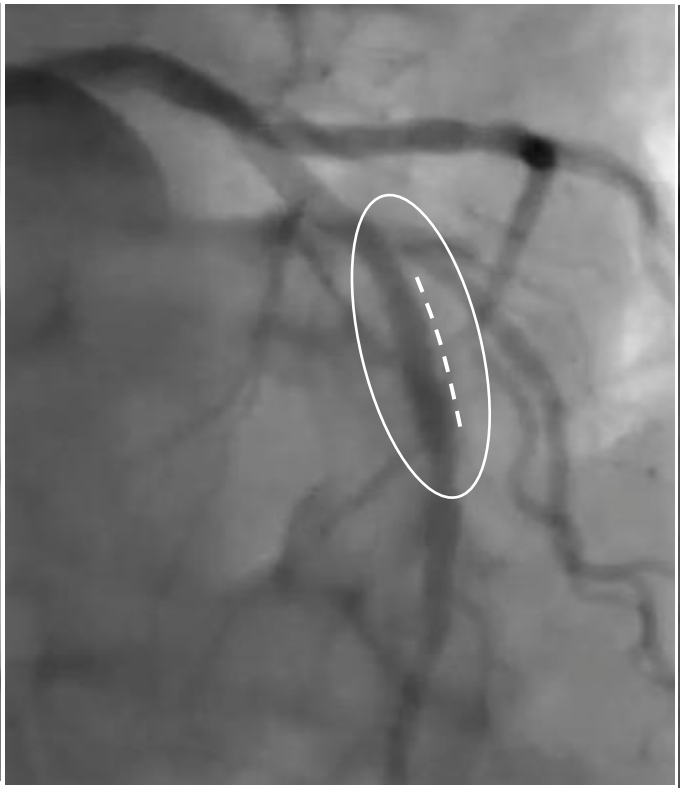
6 Month Follow-up
LLL = -0.08

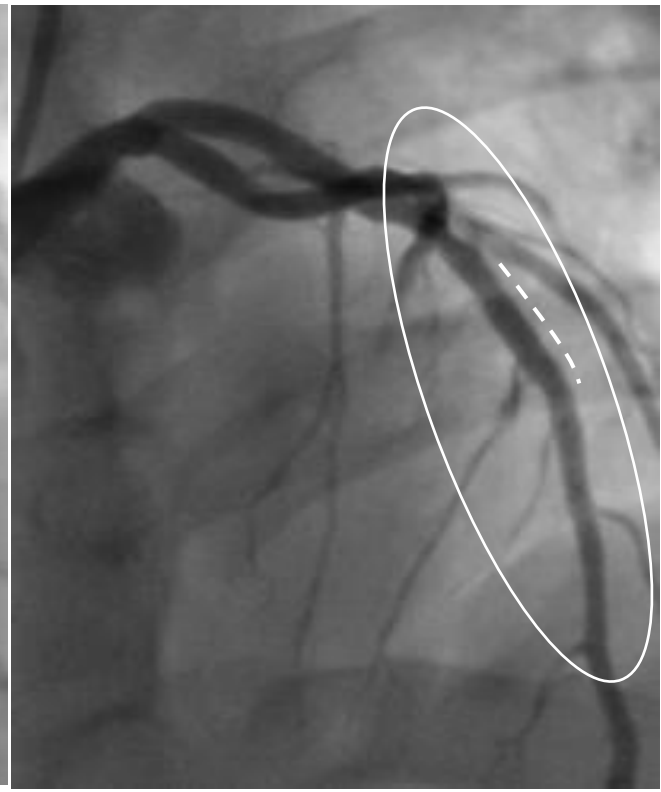
DISTAL RCA LESION			
RVD Visual / Avg QCA	2.8 / 2.48 mm	Lesion length	5 mm
RVD QCA Prox / Dist	2.41 / 2.54 mm	Stent size	2.5 x 13 mm
Pre-dilatation	2.5 mm Cutting	Virtue SAB	2.75 x 15 mm
Residual stenosis	19%		

SABRE Trial Case 06-05









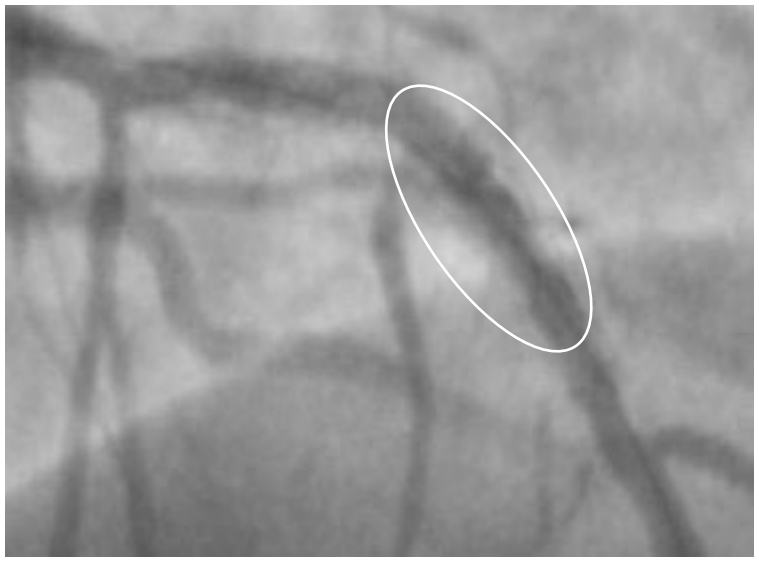
06-05 **Baseline** | **Post Lesion Preparation** | **Post Virtue SAB 3.5 x 20 mm** | **6 Month Follow-up**

LAD LESION			
RVD Visual / Avg QCA	3.5 / 2.7 mm	Lesion length	12 mm
RVD QCA Prox / Dist	2.88 / 2.42 mm	Stent size	3.5 x 15 mm
Pre-dilatation	3.25 mm Cutting	Virtue SAB	3.5 x 20 mm
Residual stenosis	23%		

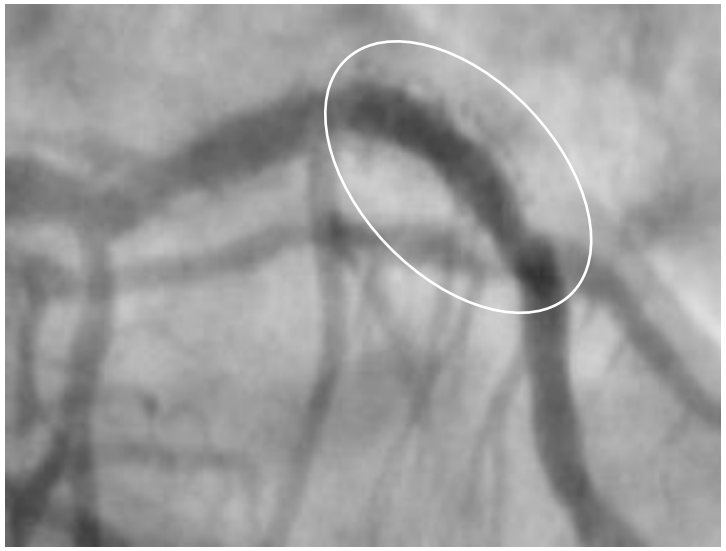
SABRE Trial Case 11-03



11-03 **Baseline**



Post Lesion Preparation



Post Virtue SAB 3.25 x 25 mm



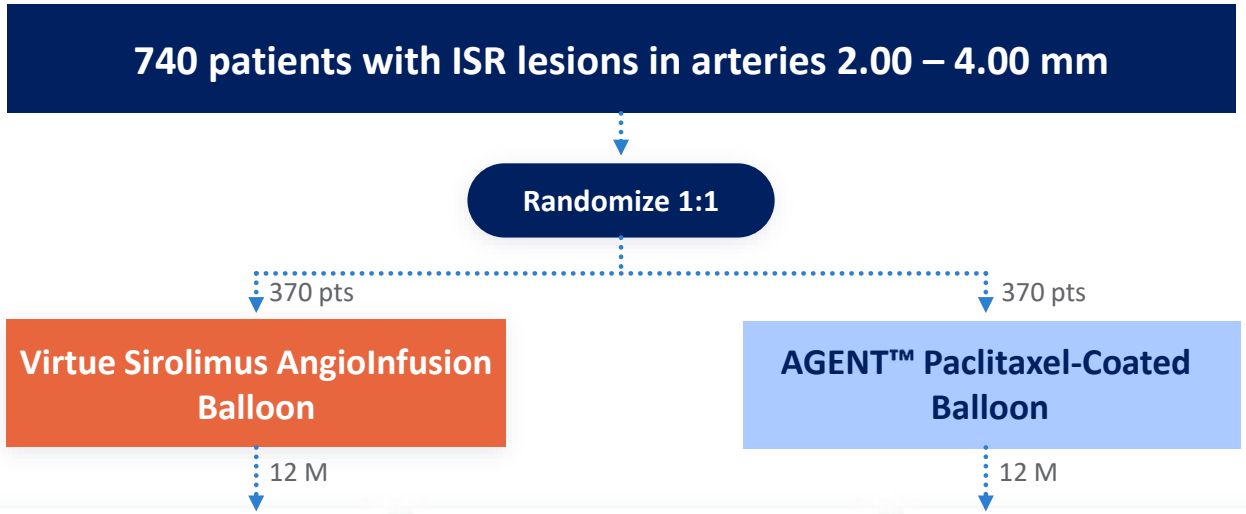
6 Month Follow-up
LLL = -0.16

LAD LESION			
RVD Visual / Avg QCA	3.0 / 2.64 mm	Lesion length	20 mm
RVD QCA Prox / Dist	2.94 / 2.33 mm	Stent size	3.0 x 33 mm
Pre-dilatation	3.00 x 20 mm Scoring	Virtue SAB	3.25 x 25 mm
Residual stenosis	20%		

Enrolling the VIRTUE ISR Coronary Pivotal Trial

Virtue Trial

- FDA IDE approved
- 1:1 RCT vs AGENT DCB
- N = 740
- Primary endpoint: 12-month TLF
- Actively enrolling trial participants in up to 100 sites
- Enrollment completion expected by end of 2027



PRIMARY ENDPOINT

Target Lesion Failure (TLF) at 12 months

ANALYSIS

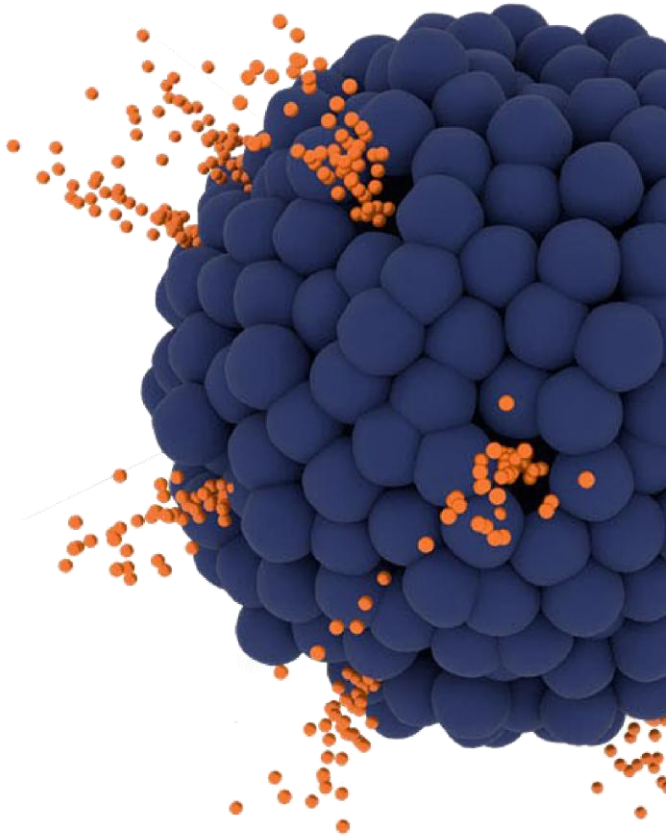
- Non-inferiority comparison
- Superiority test upon confirming non-inferiority

FOLLOW-UP

Clinical follow-up out to 5 years

Virtue® SAB Summary

- Coatings for drug delivery limit dose, lose drug in transit, transfer unevenly & rely on surface diffusion
- Virtue SAB is a first-of-its-kind drug delivery system designed to
  - Provide **large liquid volume infusion** of SirolimusEFR™ for immediate transmural distribution
  - Designed to **saturate** binding sites in the vessel wall **to maximize inhibition & modulate inflammation**
  - **Sustained transmural sirolimus release** through the critical healing period
- Virtue SAB exceeded the published pharmacokinetics of a leading drug-eluting stent
- In the SABRE Trial, Virtue SAB demonstrated compelling safety & efficacy
- Virtue ISR Trial currently enrolling (NCT07045194)





Have a Question?

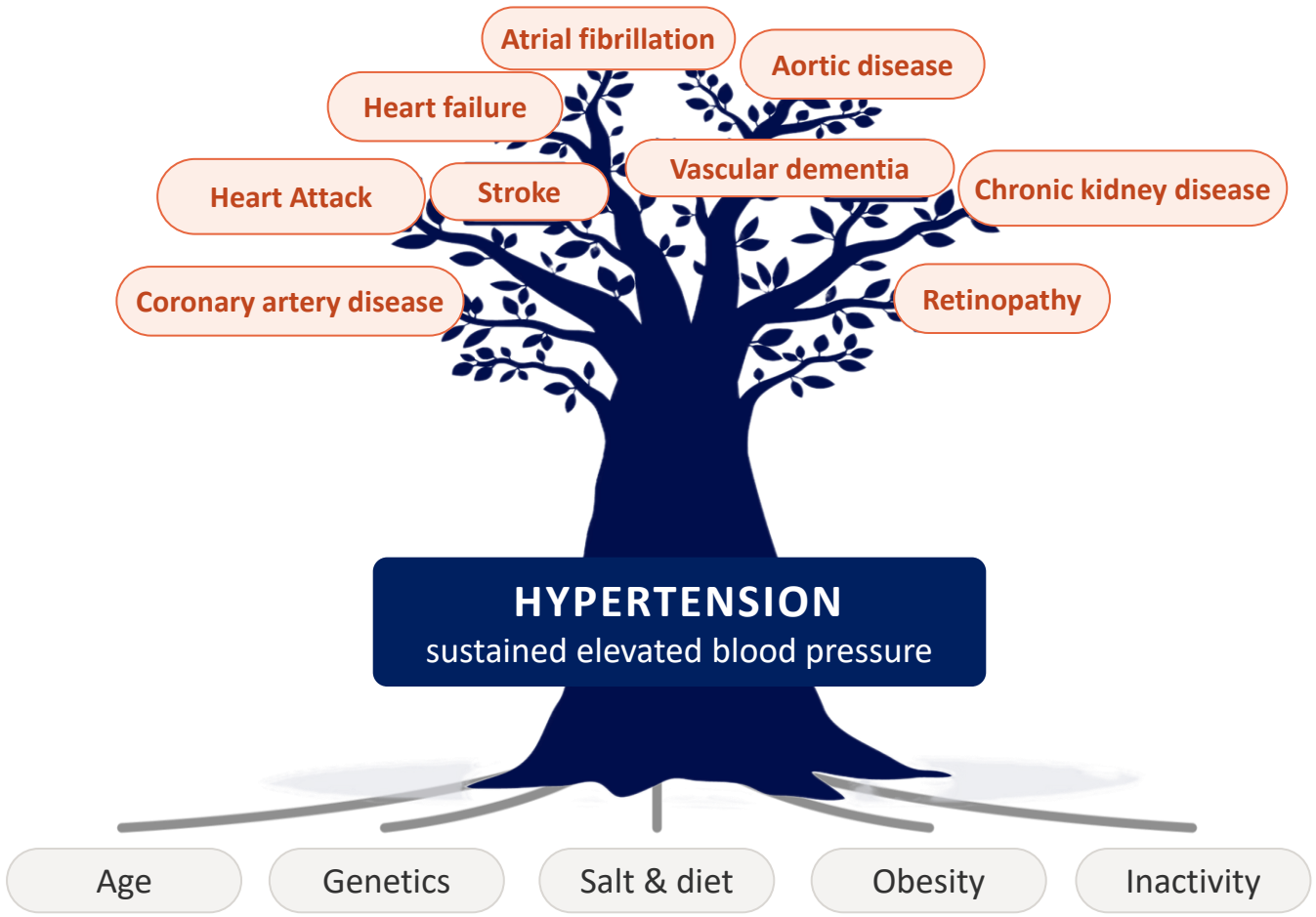
Scan the QR code to submit.

AVIM THERAPY

Atrioventricular Interval Modulation Therapy – Unmet Need, Medtronic Collaboration, Target Population & Expansion Opportunity

Hypertension is the Trunk of the Tree of Cardiovascular Disease

Every Major Cardiovascular Disease Grows from the Same Trunk: Sustained Elevated Blood Pressure



1.4B adults 30-79 living with HTN worldwide; ~1 in 4 is controlled

#1 modifiable risk factor for cardiovascular disease and premature death

10.8M deaths per year attributable to elevated systolic blood pressure

Treating hypertension can have broad impact on cardiovascular disease

Sources: WHO Global Report on Hypertension (2023); GBD 2019 Risk Factors Collaborators, Lancet 2020.

We are Targeting Patients who Need a Pacemaker, in Partnership with the Global Leader

Hypertension is #1 Comorbidity in Pacemaker Patients who are Older and Higher-risk

LAUNCH MARKET - TARGET PATIENT PROFILE

>1M

patients per year who receive pacemakers also have hypertension



Hypertension

#1

comorbidity in the pacemaker population

Pacemaker patients are older & at higher cardiovascular risk

Medtronic

GLOBAL LEADER IN CARDIAC PACING

- Exclusive global rights to pacemaker-indicated patients
- Incorporating AVIM Therapy in next-gen transvenous device (and in potential future leadless technology)
- Responsible for regulatory approvals, manufacturing and global sales, marketing & support

Pacemaker-indicated patients with uncontrolled hypertension are an ideal initial target for AVIM Therapy

Our Target Expansion Patients Have a Similar Profile to Our Launch Patients

Older, High-risk, Hypertensive Despite Medication; the Only Difference is Whether They Need a Pacemaker Today

LAUNCH MARKET - TARGET PATIENT PROFILE

>1M

patients per year who receive pacemakers also have hypertension



Hypertension

#1

comorbidity in the pacemaker population

Pacemaker patients are older & at higher cardiovascular risk

SIMILAR PATIENT PROFILE

EXPANSION MARKET - SIMILAR PATIENT PROFILE

>3.7M

annual addressable older, high-risk, comorbid patients with uncontrolled HTN[1]



Hypertension

77%

of adults with HTN remain uncontrolled[2]

Similar patient profile, no current pacemaker indication

Same age. Same risk. Same uncontrolled hypertension.

[1]Based on Company estimates. [2]World Health Organization, Global Report on Hypertension 2025 (~23% of adults aged 30–79 with hypertension have it controlled), .

Our Target Expansion Patients Have a Similar Profile to Our Launch Patients

Older, High-risk, Hypertensive Despite Medication; the Only Difference is Whether They Need a Pacemaker Today

LAUNCH MARKET - TARGET PATIENT PROFILE

>1M

patients per year who receive pacemakers also have hypertension



Hypertension

#1

comorbidity in the pacemaker population

Pacemaker patients are older & at higher cardiovascular risk

SIMILAR PATIENT PROFILE

EXPANSION MARKET – THE PATIENT PERSPECTIVE

Approximately 70% of surveyed patients are willing to undergo device implant to receive AVIM Therapy

Survey of 64 patients[1]

Preliminary research shows that patients have a substantial **interest in AVIM Therapy**

[1]Adapted from ZS Associates Primary Research Quantitative Survey on Behalf of Orchestra BioMed, October 2026, N=64. Patient cohorts included borderline pacemaker need with hypertension, post-TAVR w hypertension, post stroke, uncontrolled hypertension, heart failure with preserved ejection fraction, and abdominal aortic aneurysm patients.

AVIM Therapy: Physician Presenters



VIVEK Y. REDDY, MD

Director of Cardiac Arrhythmia Services, Mount Sinai Fuster Hospital and Mount Sinai Health System

Professor of Medicine (Cardiac Electrophysiology), Icahn School of Medicine at Mount Sinai

- Executive Chairman of the BACKBEAT Study Steering Committee & Chairman of Orchestra BioMed - Bioelectronic Therapies Scientific Advisory Board
- Internationally renowned cardiac electrophysiologist, leading a team of physician-scientists pioneering cardiovascular therapies
- Lead investigator of numerous high-impact multinational clinical trials exploring new technologies and approaches to treating cardiac arrhythmias
- Performed the world's first leadless pacemaker implant (2011) and world's first catheter-based pulsed field ablation procedure (2018)



MARAT FUDIM, MD, MHS

Associate Professor of Medicine, Duke University School of Medicine

Advanced heart failure, Duke University Medical Center; Duke Clinical Research Institute

- Member of Orchestra BioMed - Bioelectronic Therapies Scientific Advisory Board
- Internationally renowned Advanced Heart Failure Cardiologist whose research interests include advanced heart failure and HFpEF
- Medical Director of the Duke Heart Failure Research Unit and Remote Monitoring Clinic, and Director of the Duke HFpEF Clinic
- Inaugural Director of Digital Health for the Duke Clinical Research Institute and Chair of Devices in Heart Failure Task Force for the Heart Failure Society of America
- Won the 2021 American College of Cardiology Douglas Zipes Distinguished Young Investigator Award

AVIM THERAPY

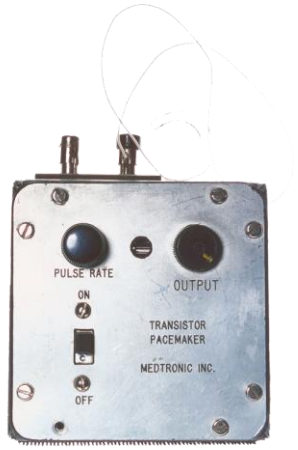
Atrioventricular Interval Modulation Therapy – Mechanism of Action, Clinical Evidence, and the BACKBEAT Trial

Vivek Reddy, MD, Executive Chairman, BACKBEAT Trial Steering Committee; Director of Cardiac Arrhythmia Services, Mount Sinai Hospital and Mount Sinai Health System

AVIM Therapy in Harmony with the Current Trends in Cardiac Pacing

TRADITIONAL PACING

- Life-saving treatment for bradycardia
- Devices are smaller & connected
- Decades of **minimizing unnecessary pacing & reducing complications**



First Medtronic Pacemaker - 1957



Medtronic Azure™ Today



Medtronic Micra™ Leadless

CONDUCTION SYSTEM PACING

- Conduction system pacing (CSP) improves patient safety
- Awakening clinical interest in new therapeutic applications





Medtronic SelectSecure™ Model 3830

Medtronic Vitalis Pacemaker Platform – Today
(CE Mark, not FDA approved)

More Than a Decade of R&D Driving AVIM Therapy to Pivotal Data

PRECLINICAL & FIRST-IN-HUMAN | **RANDOMIZED CLINICAL EVIDENCE** | **PARTNERSHIP & PIVOTAL TRIAL**

2012

Feasibility Study in Canine HTN Model

Preclinical proof of concept

Acute Feasibility Study in Subjects with HTN

First acute mechanistic evidence in humans

2016

MODERATO I First-in-Human Implant Pilot 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 late-breaking presentation at TCT

Cardiovascular Research Foundation®

2021

MODERATO II Two-Year & ISH Results

Presented at TCT

Cardiovascular Research Foundation®

Peer-reviewed publication of MODERATO II results

Journal of the American Heart Association

American Heart Association.

2022

Strategic Collaboration with Medtronic

Development and commercialization of investigative AVIM Therapy for hypertensive pacemaker patients

Medtronic

2024 - PRESENT

PIVOTAL

BACKBEAT Pivotal Trial

Prospective, multi-center, randomized, controlled, double-blind pivotal trial of AVIM Therapy

Surpassed full enrollment in September 2026

Targeting primary data readout in Q2 2027

AVIM Therapy: A Potent Hypertension Therapy Delivered By a Pacemaker

Designed to **Lower Blood Pressure** and **Improve Cardiac Function** through Well-Characterized Mechanisms

IMMEDIATE EFFECT

Short AV delays reduce blood pressure

Short AV intervals reduce ventricular filling and cardiac preload, **driving an immediate, substantial drop in systolic pressure**

SUSTAINED EFFECT

Longer AV delays maintain BP reduction

Interspersed longer AV intervals engage the baroreceptor reflex to modulate autonomic tone and reduce afterload, **maintaining the blood pressure reduction over time**

KEY ADVANTAGES

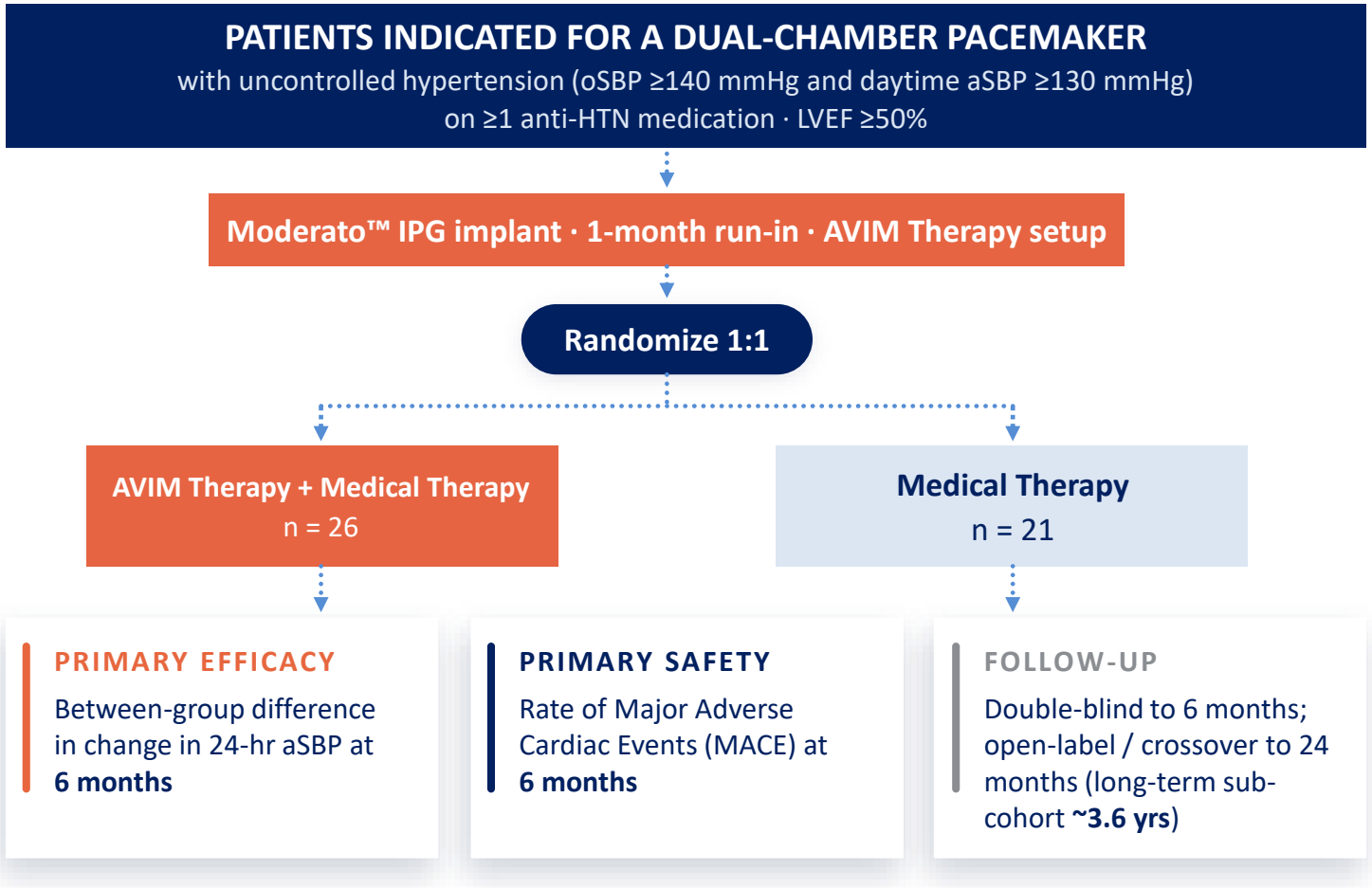
- Delivered on a **standard dual-chamber pacemaker**
- Programmable & **not dependent on patient adherence**
- Synergistic with **conduction system pacing**

The MODERATO II Study – Informed the Design of BACKBEAT

MODERATO II

RANDOMIZED, DOUBLE-BLIND PILOT STUDY

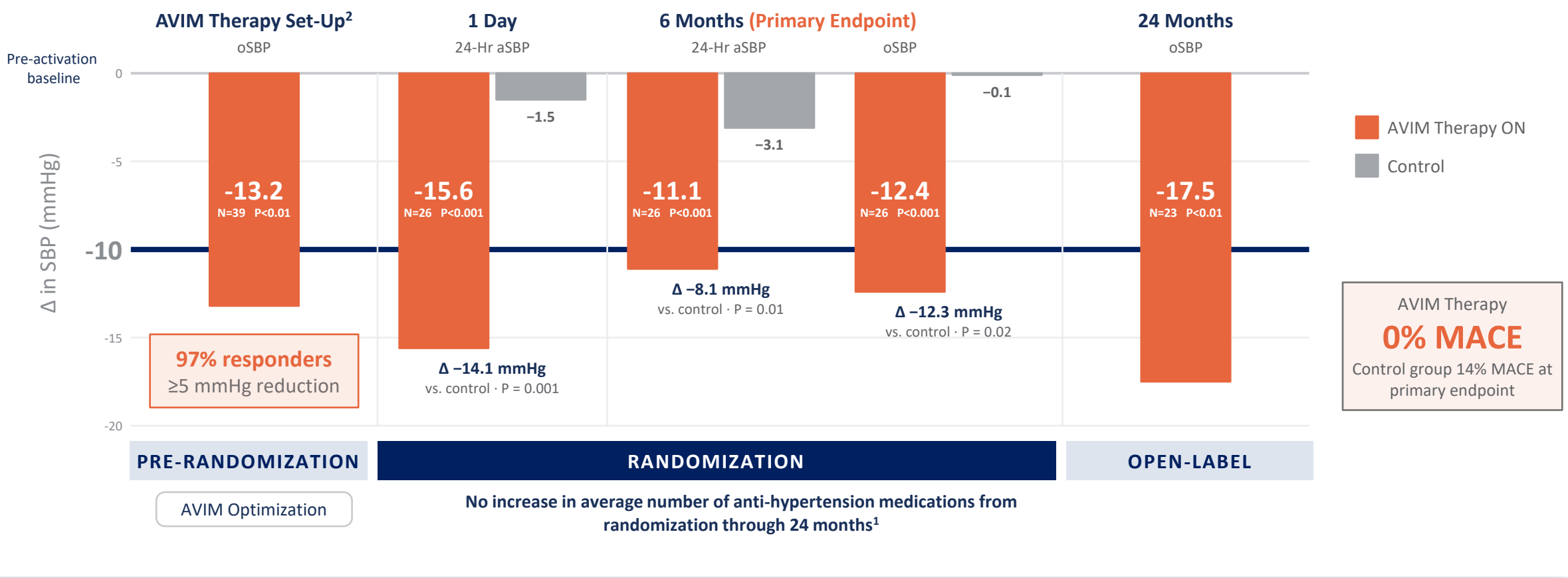
- Randomized 1:1, double-blind, controlled
- 47 patients randomized after a 1-month run-in
- Multi-center: 13 sites across 7 countries in Europe
- Intended to inform the design and power of the BACKBEAT pivotal trial



Sources: Kalarus et al., JAHA 2021;10:e020492; Burkhoff, MODERATO II 2-Year Results, TCT 2021. Definitions: aSBP (ambulatory systolic blood pressure), oSBP (office systolic blood pressure), LVEF (left ventricular ejection fraction), MACE (major adverse cardiac events), IPG (implantable pulse generator).

MODERATO II Demonstrated Immediate, Substantial and Sustained BP Reduction

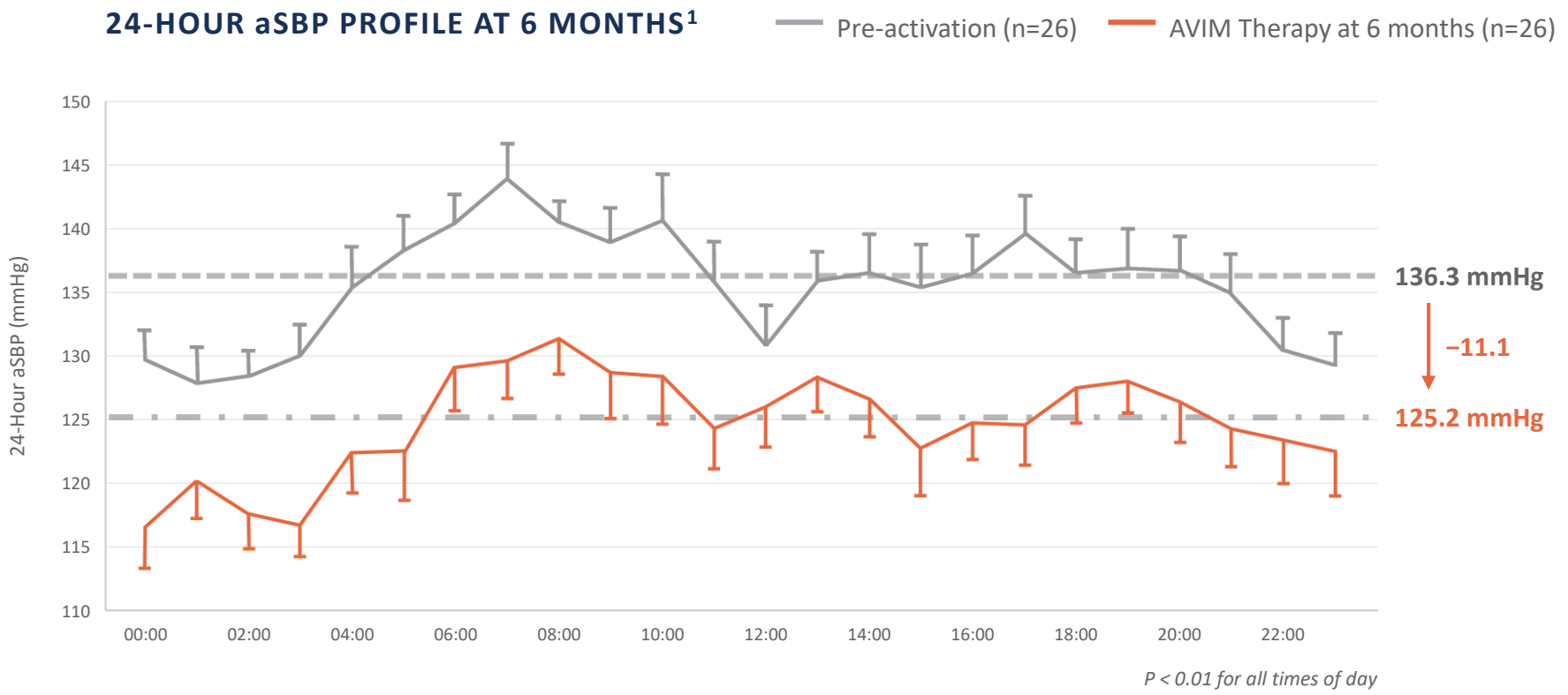
AVIM Therapy **Significantly Reduced Systolic Blood Pressure** Compared to Control with No Medication Changes & Low MACE[1]



[1]Kuck, AVIM Therapy as a Treatment for Hypertensive Heart Disease, HRS 2026. [2]Includes AVIM therapy and control patients at pre-randomization using BACKBEAT Trial set-up methodology. Control N=21; Δ = between-group difference, AVIM Therapy vs. control. Definitions: MACE (Major Adverse Cardiac Events), aSBP (ambulatory Systolic Blood Pressure), oSBP (office Systolic Blood Pressure), Hr (Hour).

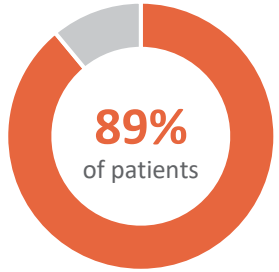
MODERATO II: High Therapy Response with the Daily BP Pattern Preserved

Significant Reduction in 24-hour aSBP **while Preserving the Normal BP Pattern** Throughout the Day



Avg SBP at 6 months[2]
125.2 ± 12.6 mmHg

Achieved aSBP <140 mmHg



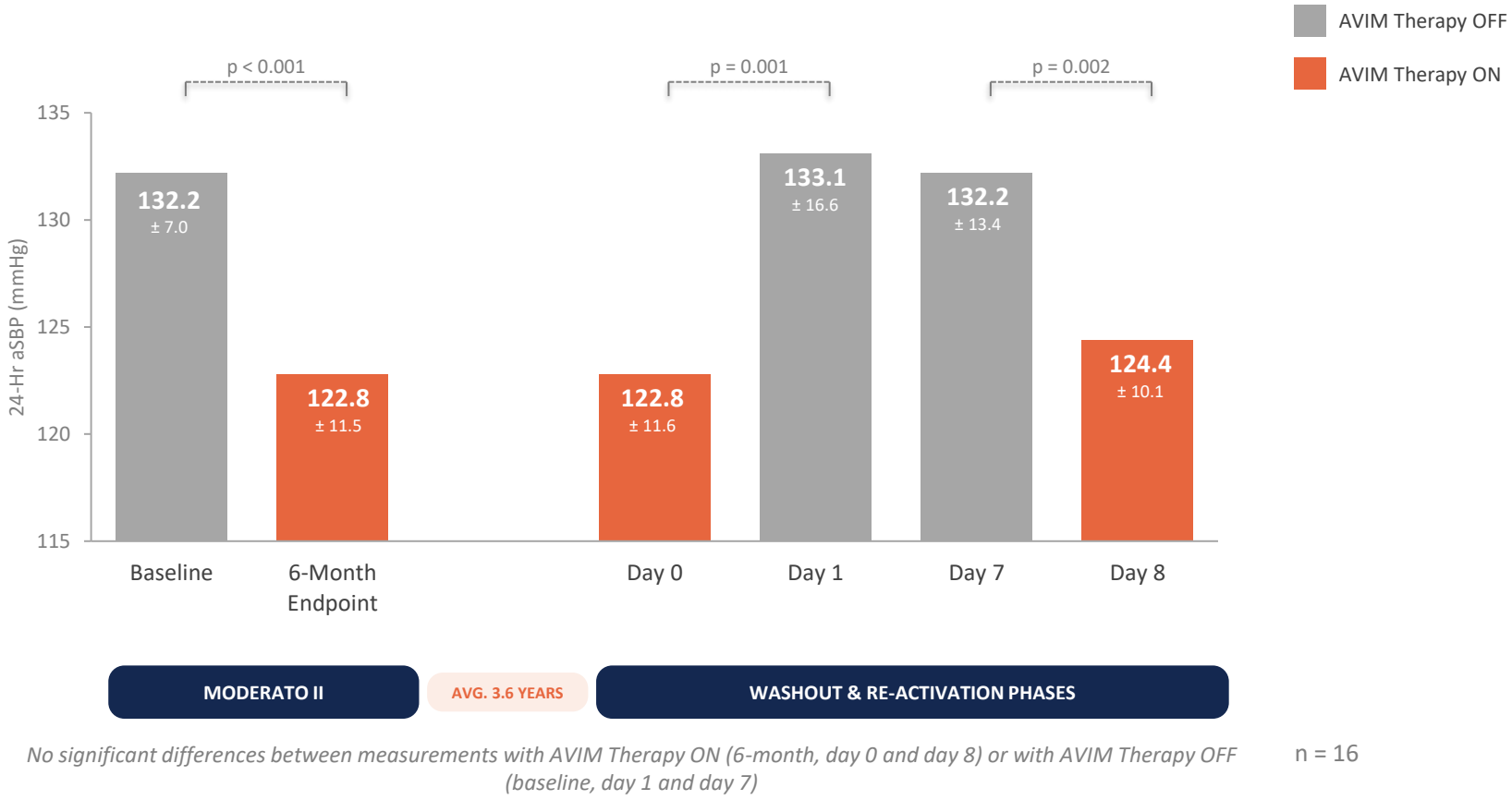
[1]Burkhoff, MODERATO II Study 2-Year Results, TCT 2021. [2]Kalarus Z, et al., J Am Heart Assoc. 2021;10:e020492. Definitions: BP (Blood Pressure), aSBP (ambulatory Systolic Blood Pressure).

AVIM Therapy's Effect is Sustained and Fully Reversible Years Later

Long-term MODERATO II Patients (avg. 3.6 years) **De-activated and Re-activated**: Sustained, Reproducible aSBP Reduction[1]

Patients with long-term AVIM Therapy de-activated & re-activated

- **No increase** in avg. number of meds across study phases
- **Sustained reduction** in SBP for an avg 3.6 years
- **Potential halt in hypertensive heart disease progression:** aSBP returned to baseline pressure after ~3.6 years
- **No rebound hypertension**



No significant differences between measurements with AVIM Therapy ON (6-month, day 0 and day 8) or with AVIM Therapy OFF (baseline, day 1 and day 7)

n = 16

[1]Fischer, Atrioventricular Interval Modulation Therapy for Management of Hypertension, HRX 2025. 2. Merkely B, et al. Time Course of Changes in Blood Pressure Following Discontinuation and Reactivation of Chronic Atrioventricular Interval Modulation (AVIM) Therapy. JACC: Advances 2026 (in press)
Definitions: aSBP (Ambulatory Systolic Blood Pressure), AVG (Average).

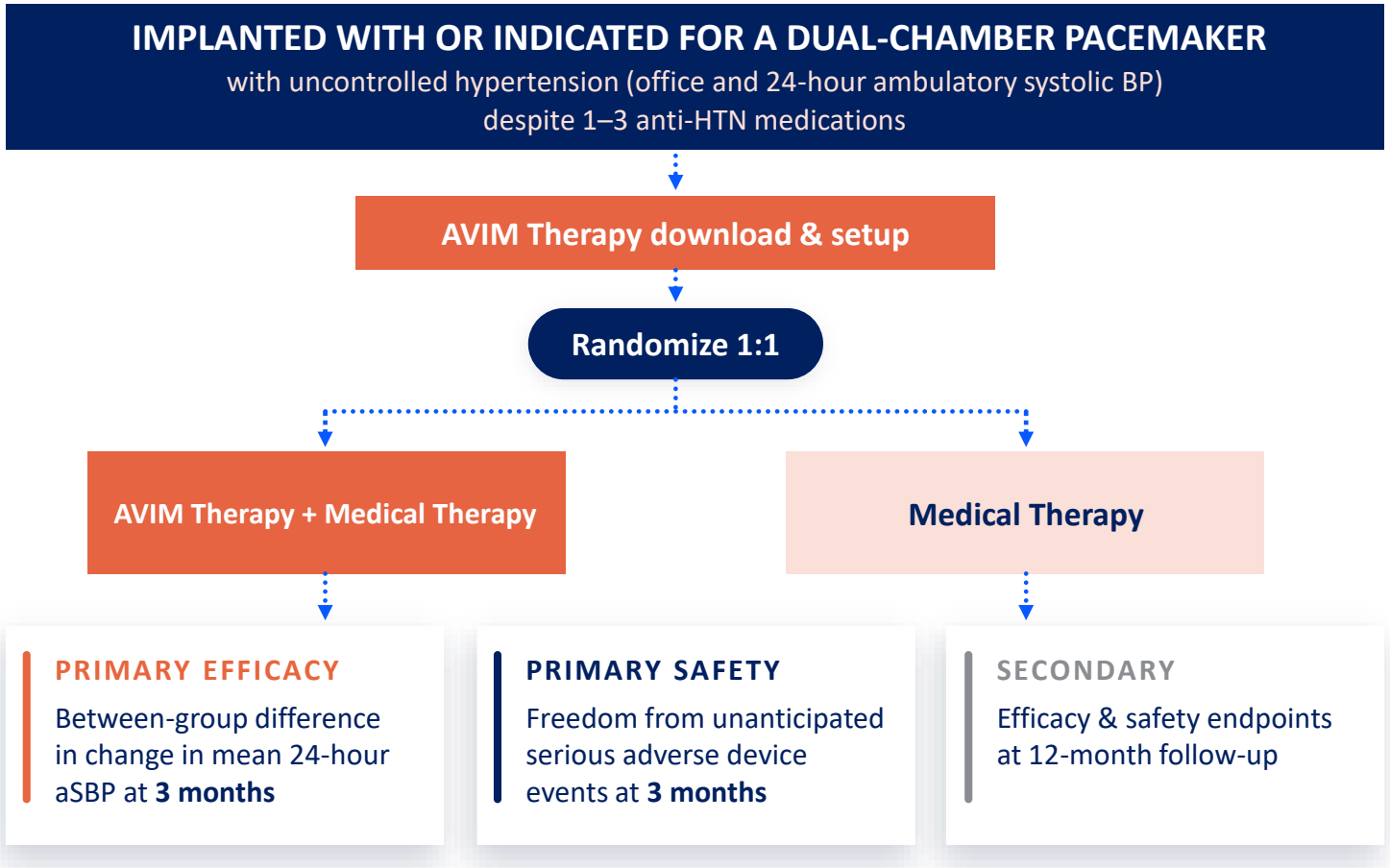
The BACKBEAT Global Pivotal Trial – Enrollment Completed

BACKBEAT
GLOBAL PIVOTAL STUDY

- Double-blind, randomized (1:1)
- 92 sites in 15 countries; 50% of subjects from the US
- 349 subjects randomized
- >95% statistical power (safety & efficacy); based on 284 evaluable randomized subjects

Orchestra BioMed™ Medtronic

Sponsored by Orchestra BioMed in collaboration with Medtronic



The BACKBEAT Trial - Large, Robust, and Broadly Representative

BACKBEAT Patients are Expected to be Representative of Real-world Patients

PACEMAKER INDICATIONS
Any dual-chamber pacemaker indication

- Sick sinus syndrome
- AV block (all)
- New implants, existing implants and generator changes

TARGET POPULATION
Typical characteristics of pacemaker patients with HTN

- Age: ~75 yrs average
- Expected comorbidities:
  - Diabetes
  - Coronary Artery Disease
  - Prior MI or Stroke
  - Atrial Fibrillation (<10%)
  - Heart Failure (NYHA I & II)

REAL-WORLD USE
Therapy activation not tied to implant procedure

- AVIM can be activated soon after implant, or years after implant
- No adjustments to settings required
- Therapy can be turned off and BP effects are fully reversible

Commercial Device: AVIM Therapy Integrated into Device and Programmer

AVIM Therapy Fits into Current Pacemaker Workflows



AVIM Therapy Can Be Activated at Implant or Any Time After

Significant Expansion Opportunity Beyond the Pacemaker Market

AVIM Therapy Can Potentially Expand the Patient Population for Pacing while Leveraging Emerging Device Technologies

EXPANSION MARKET - SIMILAR PATIENT PROFILE

>3.7M

annual addressable older, high-risk, comorbid patients with uncontrolled HTN[1]



Hypertension

77%

of adults with HTN remain uncontrolled[2]

- ✓ Typical Age: >65
- ✓ Expected comorbidities:
  - Diabetes
  - Coronary Artery Disease
  - Prior MI or Stroke
  - Atrial Fibrillation
  - HFpEF

Pacemaker Indication?

AVIM THERAPY + DUAL-CHAMBER PACING FROM A SINGLE LEADLESS DEVICE

A Powerful Future Possibility

HeartRhythm

The Official Journal of the Heart Rhythm Society, The Cardiac Electrophysiology Society, and The Pediatric & Congenital Electrophysiology Society

Heart Rhythm Society SM

Dual-chamber pacing from a single leadless device: Preclinical implant and retrieval feasibility study

Jonathan P. Piccini, MD, MHS, FHRS,[1] Kaileigh Hayden, MS,[2] Alexander R. Mattson, PhD,[2] Kathryn Hilpisch, MS,[2] Kent Wika, MS,[2] Kyoko Soejima, MD[3]

ABSTRACT

BACKGROUND Sequential atrioventricular pacing can be accomplished with separate atrial and ventricular devices. Integration of atrial and ventricular pacing within a single leadless device represents a novel approach to dual-chamber pacing (DDD).

OBJECTIVE This study aimed to demonstrate the feasibility of single-device, leadless DDD in an ovine model by assessing implant safety, chronic electrical performance, and chronic device retrieval.

[1]Based on Company estimates. [2]World Health Organization, Global Report on Hypertension 2025 (~23% of adults aged 30–79 with hypertension have it controlled).

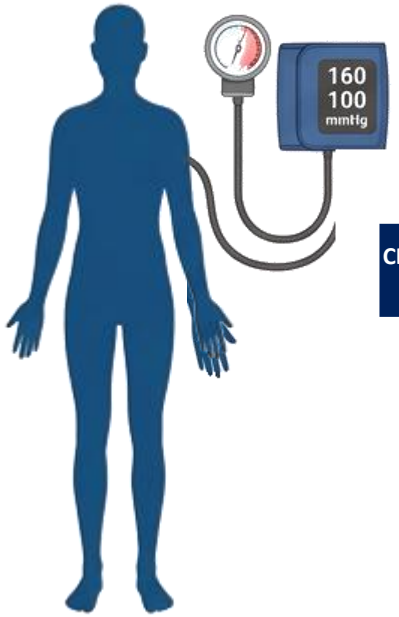
AVIM THERAPY

Hypertension, Diastolic Dysfunction and Heart Failure

Marat Fudim, MD, MHS, Associate Professor of Cardiology, Advanced Heart Failure, Duke University Medical Center

Hypertension is a Major Driver of Heart Failure[1]

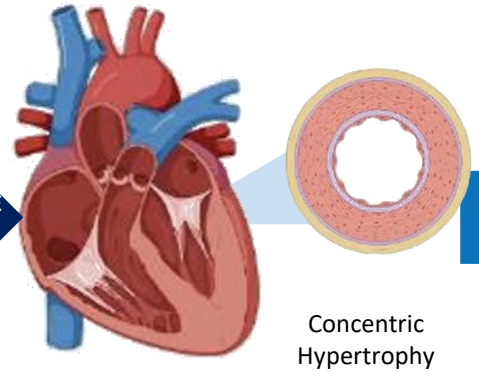
HIGH BLOOD PRESSURE (HYPERTENSION)



CHRONIC PRESSURE OVERLOAD

CARDIAC STRUCTURAL REMODELING

Hypertrophied Left Ventricle

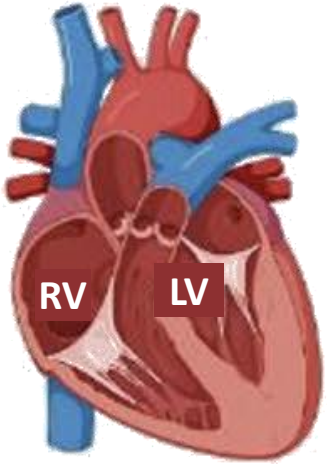


Concentric Hypertrophy

MECHANICAL DYSFUNCTION

DIASTOLIC DYSFUNCTION

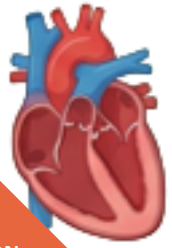
Left Ventricle struggles to relax & fill during diastole



PROGRESSION TO HF

HFpEF

(Heart Failure with Preserved Ejection Fraction - LVEF ≥50%)



Stiff, Non-compliant Heart

Rigid, thickened LV with reduced flexibility



Increased Atrial & Venous Pressure

Dilated, backing up into pulmonary circulation

[1] Adapted from Nadruz W, Shah AM, Solomon SD. Diastolic Dysfunction and Hypertension. Med Clin North Am. 2017;101(1):7-17. Redfield et al., Heart Failure With Preserved Ejection Fraction: A Review. JAMA. 2023;329(10):827-838. WHO Global Report on Hypertension 2025; GBD Risk Factor analyses.

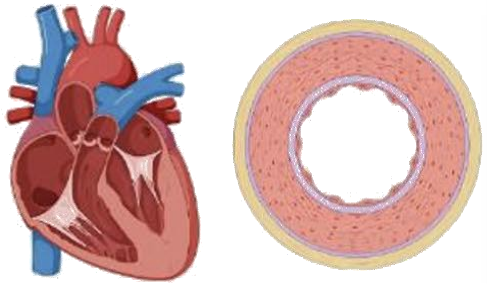
Hypertension Is a Key Driver of HFpEF

Age and Hypertension are the Two Leading Drivers of Diastolic Dysfunction

↑ Blood Pressure[1]

Structural

- Concentric LV remodeling
- Diastolic Dysfunction
- ↓ LV Compliance
- Impaired Relaxation



Vascular

- Arterial Stiffness
- ↑ Afterload
- ↑ Late Systolic Load
- Ventricular–Vascular Uncoupling

↑ LV Filling Pressures | **↑ LA Pressure** | **Pulmonary Hypertension** | **RV Dysfunction** | **Exertional Dyspnea**

The HFpEF Population[2]

~3M	people living with HFpEF in the U.S.
~80%	have hypertension
>50%	remain uncontrolled
~1.4M	**uncontrolled hypertension + HFpEF**

[1]Adapted from Arshad MS, et al. Heart Failure Reviews (2026) 31:31. [2] Based on Company Estimates.

AVIM Therapy Pressure-Volume Loop Study[1]

Evaluate the Effect of AVIM Therapy on Cardiac Function When Delivered Using Traditional and Conduction System Pacing

Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension

Milan Chovanec, MD, PhD,[a] Béla Merkely, MD, PhD,[b] Adam Sokal, MD,[c,d] Jan Petrů, MD,[a] Štěpán Královec, MD,[a] Tomáš Drtina, MD,[a] Martin Mudroch, MD,[a] László Gellér, MD, PhD,[b] István Osztheimer, MD, PhD,[b] Stanislaw Morawski, MD,[c] Yuval H. Mika, PhD,[e] Avi Fischer, MD,[e] Steven J. Evans, MD,[e] Ricardo Aviv, PhD,[e] Norbert Rosenthal, BEng,[e] Daniel Burkhoff, MD, PhD,[f] Karl-Heinz Kuck, MD,[g] Petr Neužil, MD, PhD[a]

- Pacemaker-indicated patients with uncontrolled HTN despite medical therapy
- Cardiac function evaluated using a pressure volume catheter in the left ventricle
- Blood pressure measured using a transducer placed in the aorta
- Baseline measurements acquired with intrinsic ventricular conduction
- Dual-chamber pacing and AVIM were delivered sequentially
- Paired data (baseline vs RV pacing or baseline vs AVIM Therapy) reported

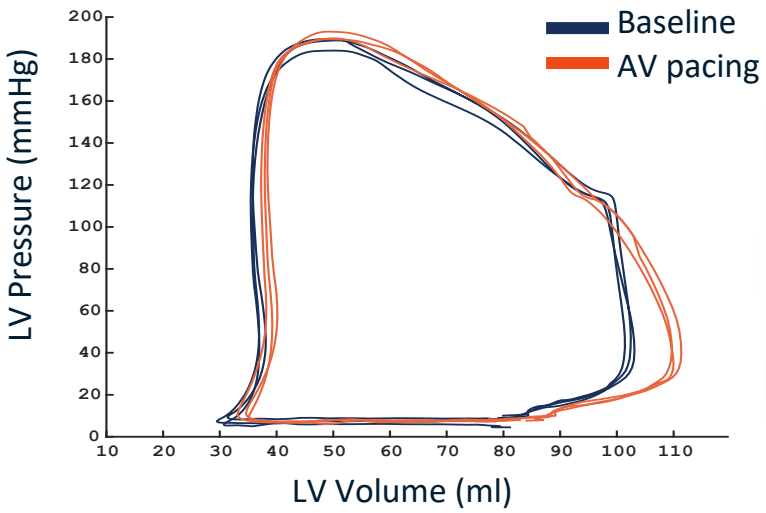
BASELINE CHARACTERISTICS (N = 16)

Number of subjects (N)	16 (7 M/9 F)
Age (yr)	70.2 ± 10.7
BP (mmHg)	
Systolic	145.9 ± 20.5
Diastolic	68.1 ± 12.0
Avg # of Anti-HTN meds	2.5
Diabetes	3 (18.8%)
History of AF	2 (12.5%)
Coronary Artery Disease	4 (25%)
Renal dysfunction	3 (18.8%)
Sinus Node Disease	11 (69%)
II° AV Block	5 (31.3%)
III° AV Block	1 (6.3%)

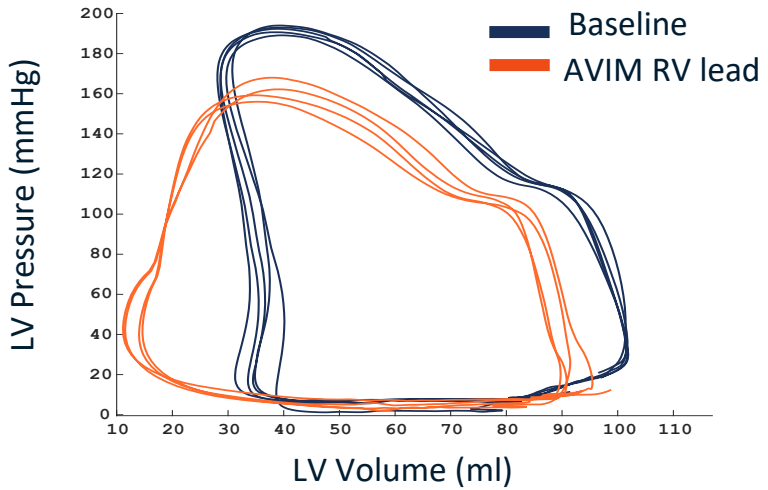
[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

AVIM Therapy PV-Loop Study Results[1]

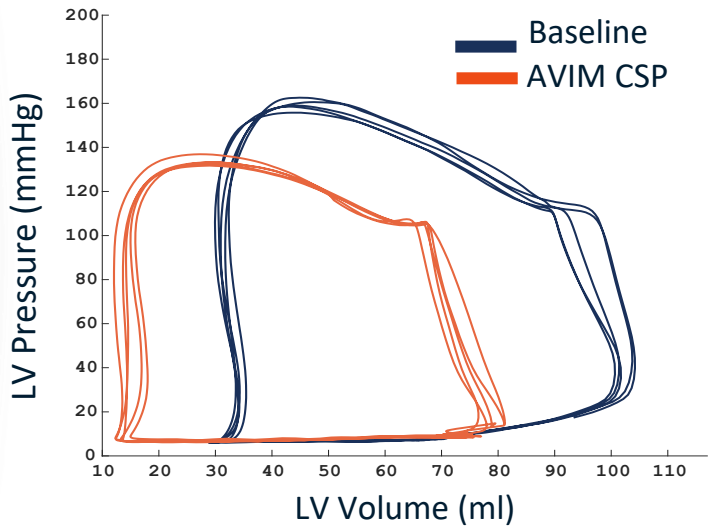
AV Sequential Pacing



AVIM - RV Lead Location



AVIM – CSP Lead Location



Decreases systolic blood pressure

Decreases intra-cardiac volume & pressure (↓ EDV, ↓ ESV)

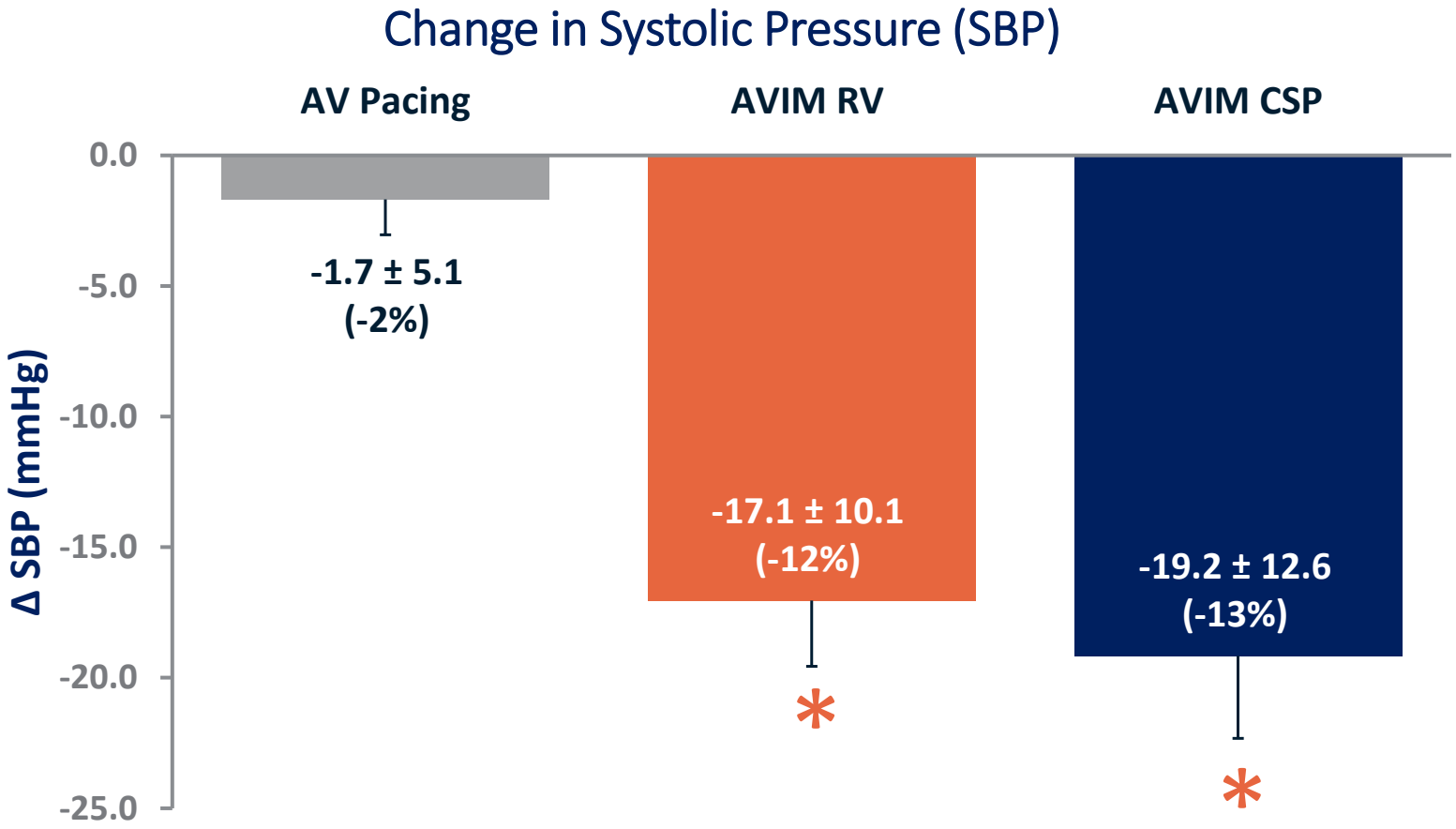
Decreases total peripheral resistance (TPR)

Reduces stroke work

[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

AVIM Therapy Demonstrated a Reduction in Systolic Blood Pressure[1]

Significant reduction in SBP with AVIM Therapy and **no significant difference between RV and CSP lead placement**



Numbers are standard deviation (SD), error bars are standard error measurements (SEM)

N=16

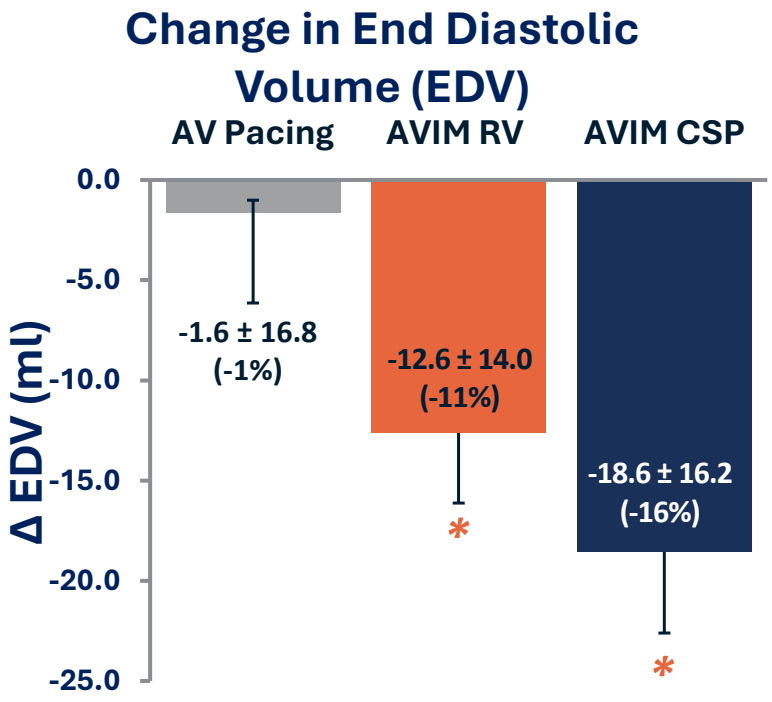
**** P <0.05 (Compared to baseline)***

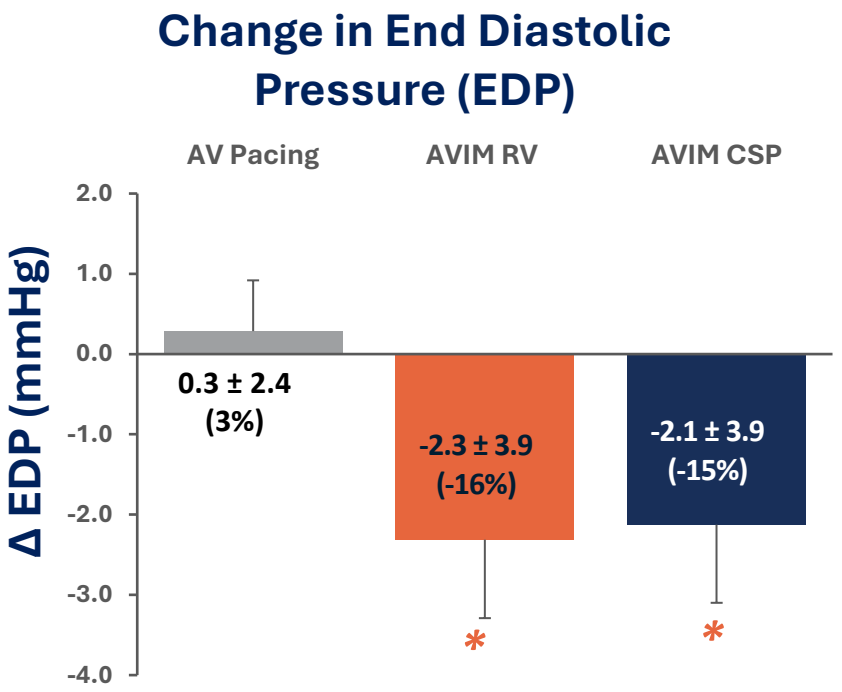
No significant difference between AVIM RV and AVIM CSP

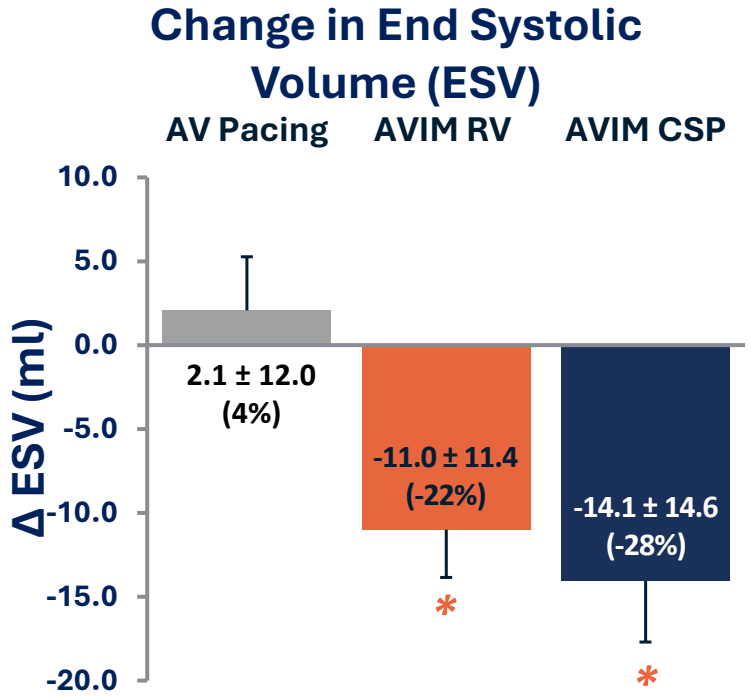
[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

AVIM Therapy has a Favorable Impact on Hemodynamics[1]

Significant Reductions in ESV, EDV and EDP







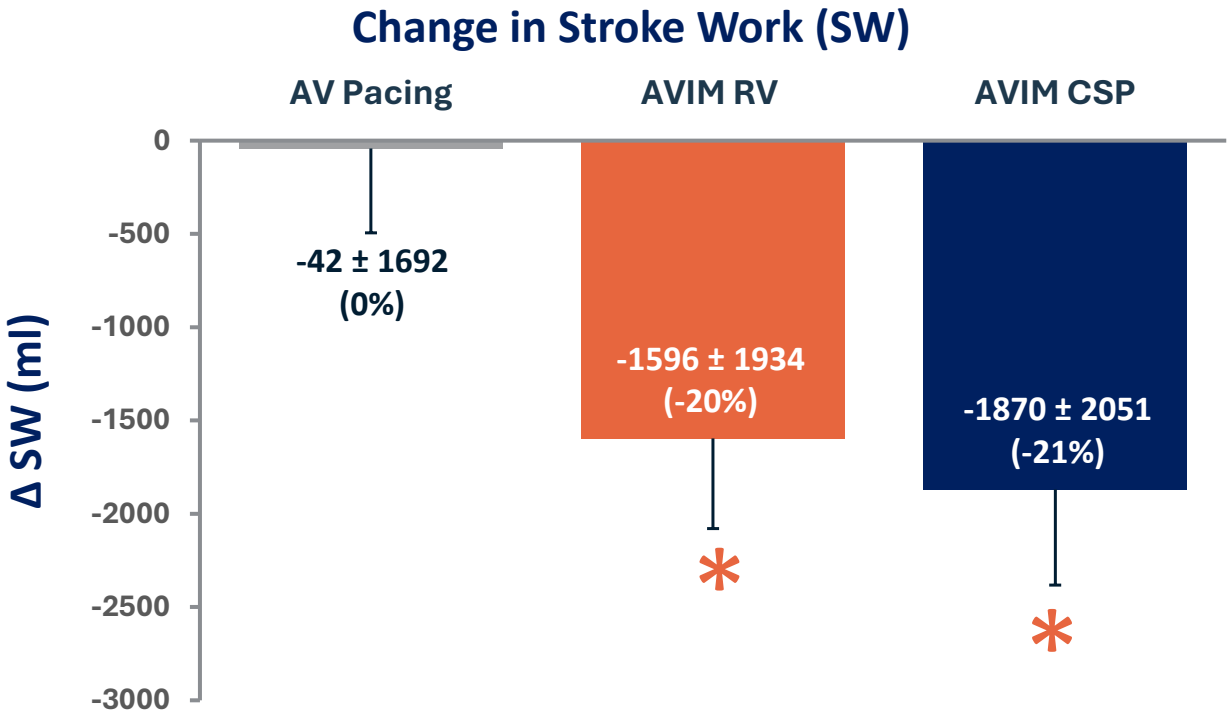
** P <0.05 (Compared to baseline)*

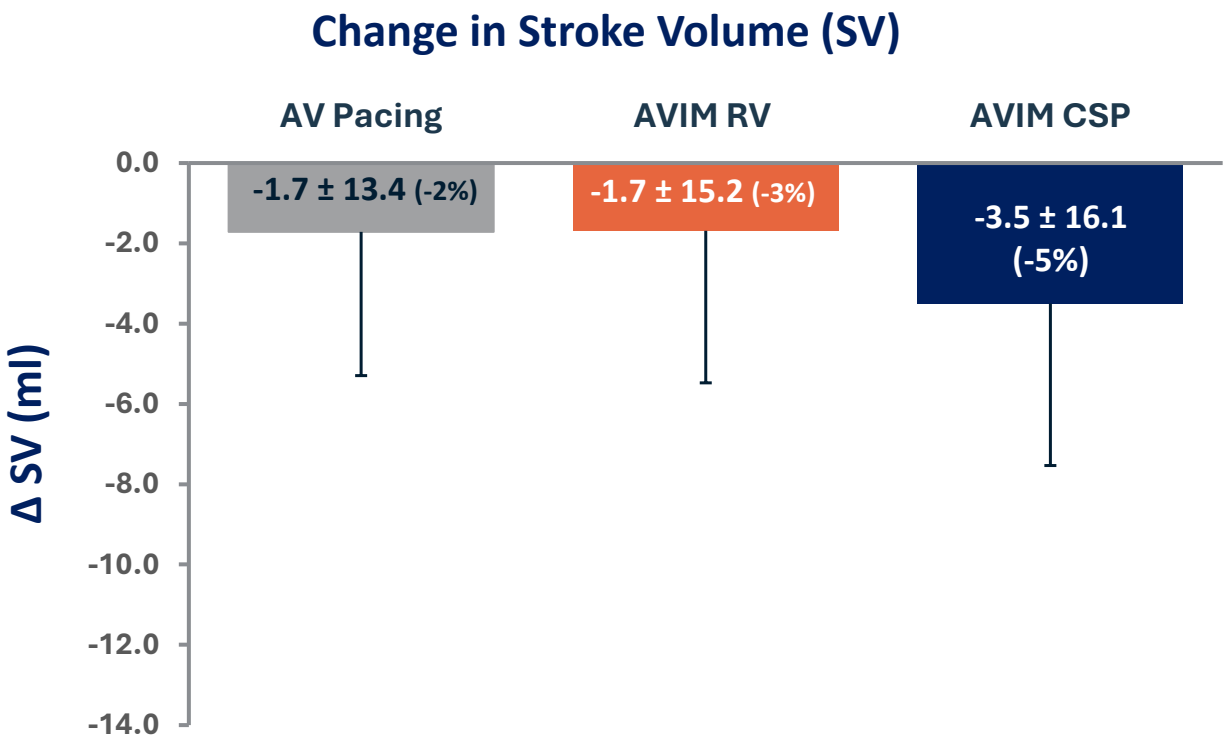
No significant difference between AVIM RV and AVIM CSP

[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

AVIM Therapy has a Favorable Impact on Hemodynamics[1]

Significant Reduction in Stroke Work (SW) without Significant Reduction in Stroke Volume (SV)





Numbers are SD, error bars are SEM

**** P <0.05 (Compared to baseline)***

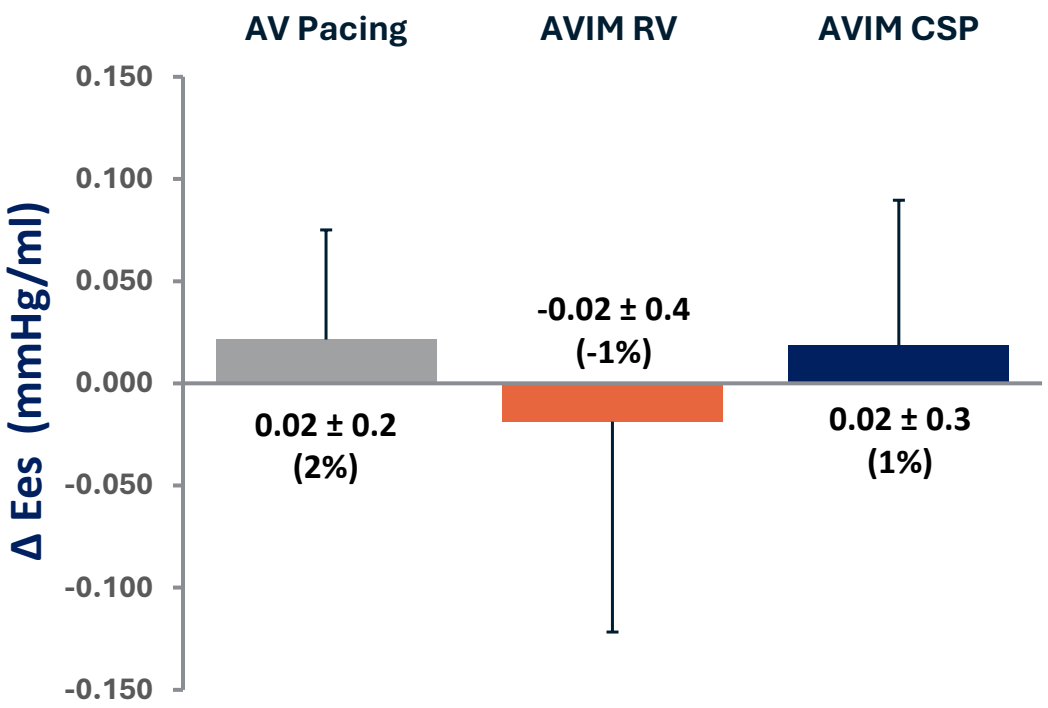
No significant difference between AVIM RV and AVIM CSP

[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

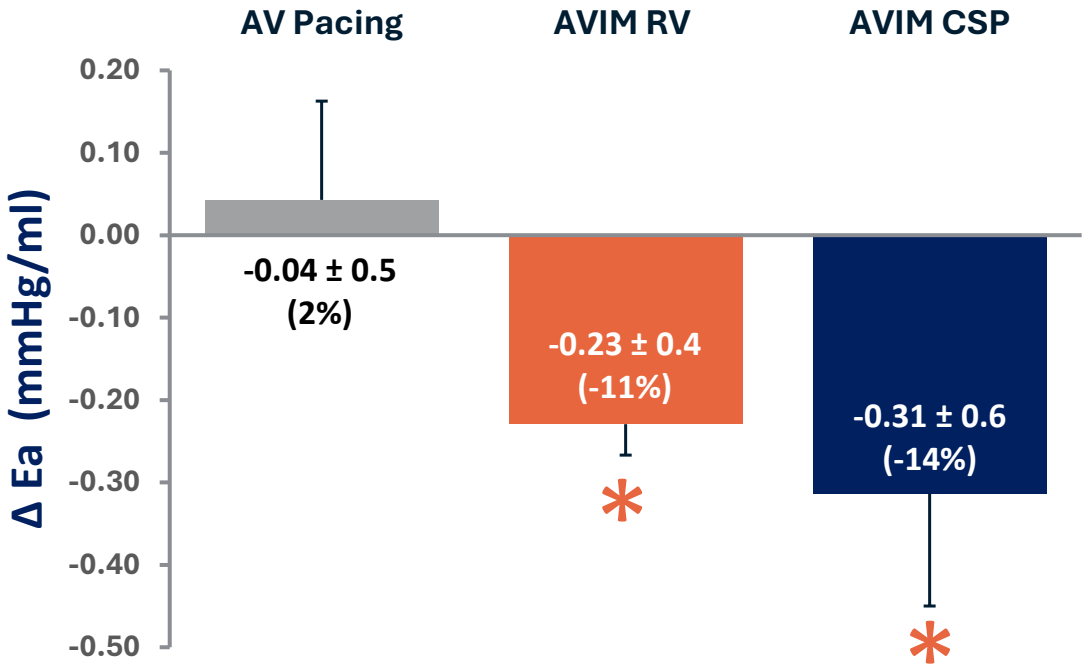
AVIM Therapy has a Favorable Impact on Hemodynamics[1]

Reduction in Total Peripheral Resistance (Ea) and No Change in Contractility (Ees)

Change in Contractility (Ees)



Change in Effective Arterial Elastance (Ea)



Numbers are SD, error bars are SEM

**** P <0.05 (Compared to baseline)***

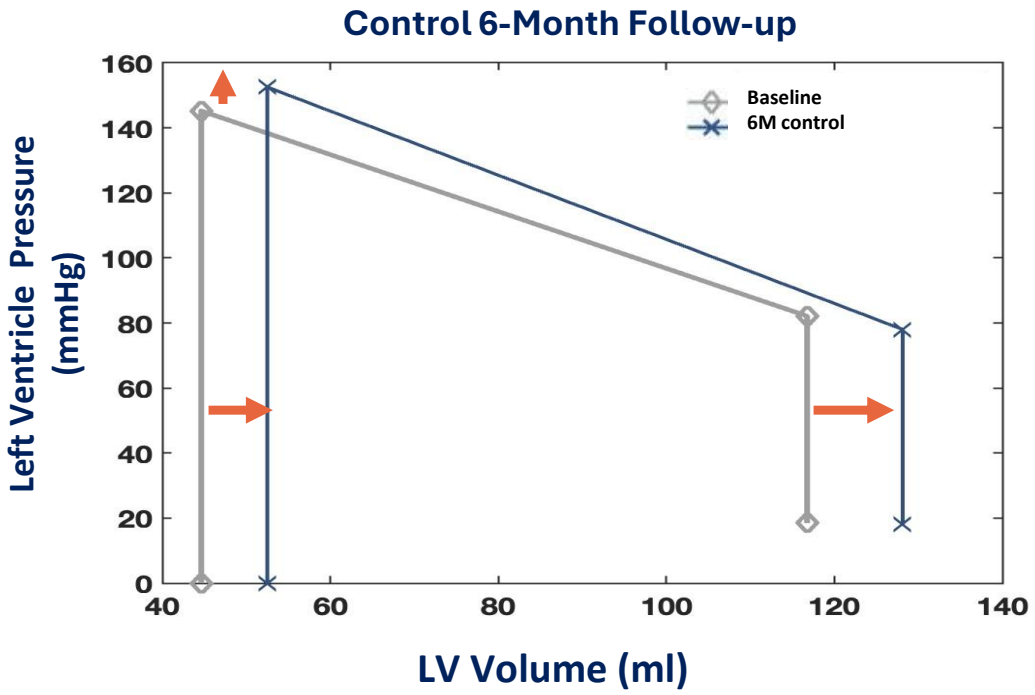
No significant difference between AVIM RV and AVIM CSP

[1]Chovanec M, et al. Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension. JACC Clin Electrophysiol. 2025 Nov;11(11):2493-2504

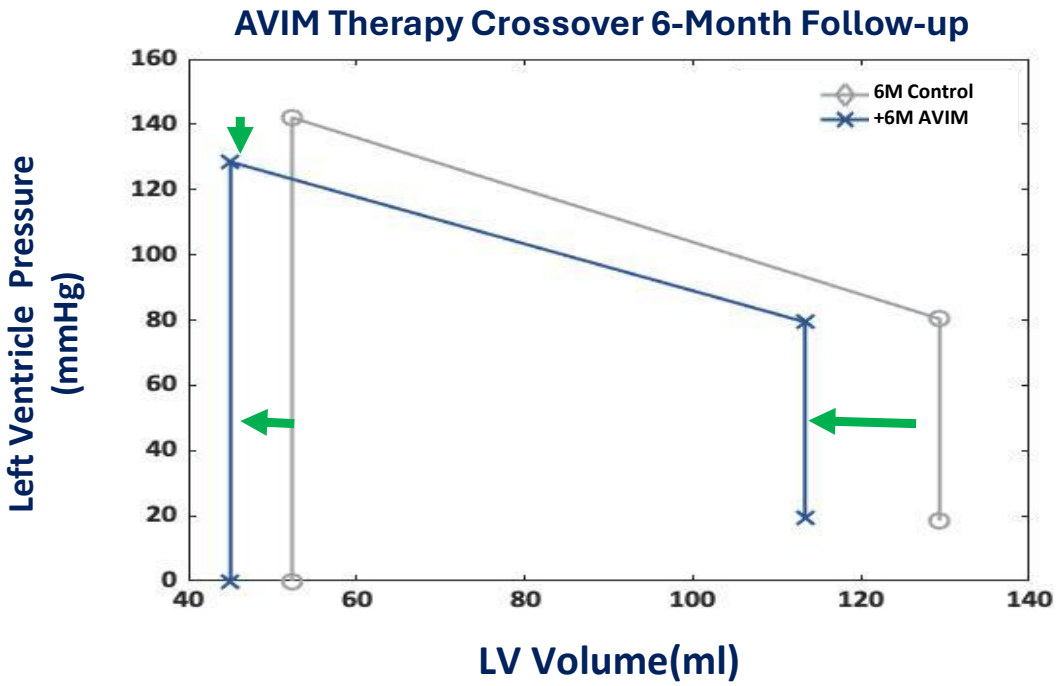
MODERATO II: Chronic, Non-Invasive PV Loops Show Favorable Effects on Cardiac Remodeling*[1]

AVIM Therapy Reverses Adverse Remodeling

Unfavorable remodeling in control patients resulted in increases in ESV, EDV, and ESP



Favorable reverse remodeling after crossover to AVIM Therapy demonstrated by reductions in ESV, EDV, and ESP**



**Paired data (N=12, N=6) ** 6 months of control followed by 6 months of AVIM therapy after crossover (12 months from baseline)*

[1]Kuck KH. Clinical Evidence Supporting Atrioventricular Interval Modulation Therapy (AVIM): Results from the MODERATO I & II Studies, EHRA 2024

Retrospective Analysis of MODERATO II Patients with Diastolic Dysfunction (DD)

Hypertension is the Leading Cause of DD. Both Conditions are Common in the **Elderly** and **Contribute to the Development of Heart Failure**

How the Analysis was Done

Retrospective, treatment-blinded analysis

MODERATO II core-lab echocardiograms reviewed with independent blinded adjudication

Classified patients as with or without DD

Using the American Society of Echocardiography guidelines – ≥ 2 of the standard criteria required*

Assessed impact of 6 months of AVIM Therapy

On SBP and echocardiographic markers of diastolic dysfunction

**ASE criteria (≥ 2 of): average E/e' > 14, or septal e' < 7 cm/sec or lateral e' < 10 cm/sec, or TR > 2.8 m/sec; LA volume index > 34 ml/m²; LVH > 1.1 cm*

61%

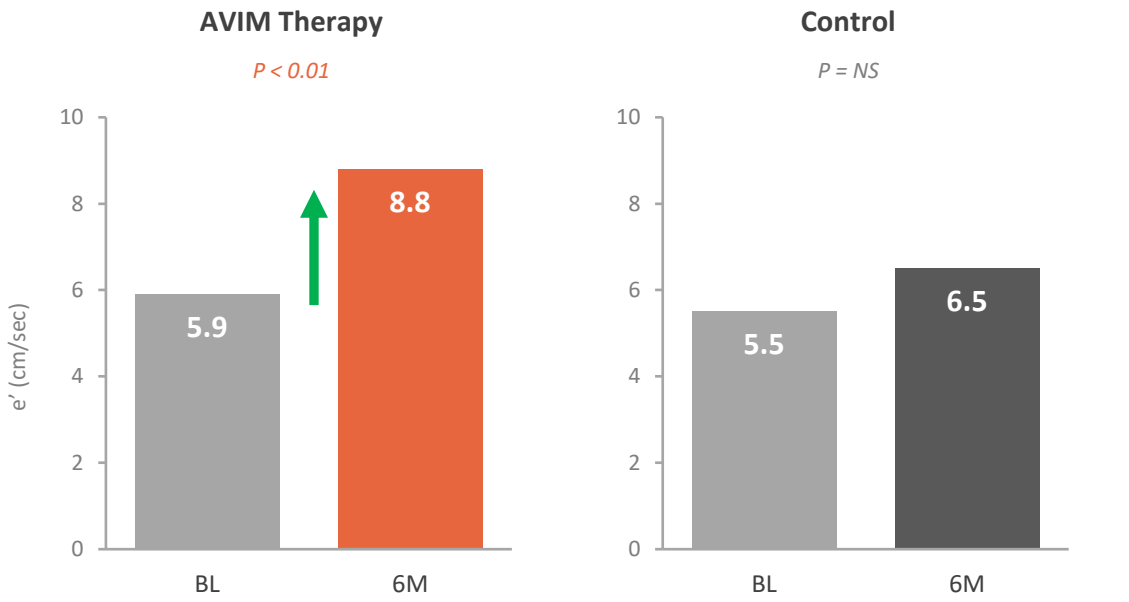
of MODERATO II evaluable subjects had echocardiographic evidence of **diastolic dysfunction (DD)**[1]

[1]Fudim M et al., Effects of Atrioventricular Interval Modulation Therapy in Subjects with Hypertension and Diastolic Dysfunction. JACC: Advances. Vol. 4, No. 7, July 2025:101896. **Definitions:** DD (Diastolic Dysfunction), SBP (Systolic Blood Pressure), ASE (American Society of Echocardiography), TR (Tricuspid Regurgitation), LA (Left Atrial), LVH (Left Ventricular Hypertrophy).

MODERATO II: Improved Diastolic Dysfunction

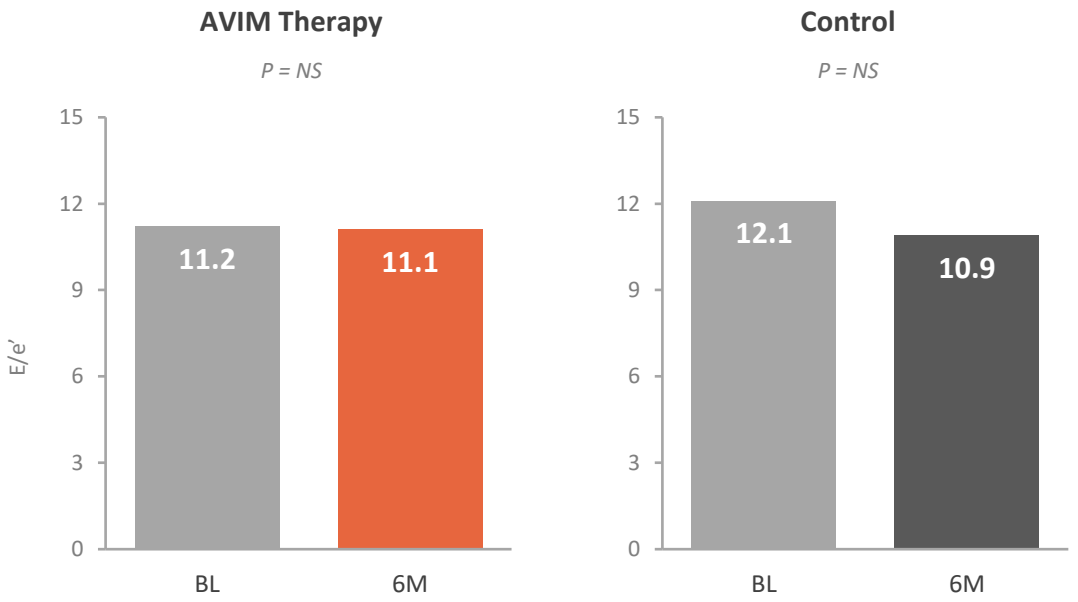
AVIM Therapy **Significantly Increased e' with Stable E/e'**, Indicating Improved Myocardial Relaxation and Passive Filling[1]

e' *Early diastolic mitral annular velocity – a marker of myocardial relaxation*



↑ e' with AVIM Therapy → improved myocardial relaxation and early LV filling

E/e' *Ratio of early mitral inflow to annular velocity – reflects LV filling pressure*



Unchanged E/e' → LV filling pressure not increased

DD+ Baseline | DD+ AVIM Therapy (n=12) | DD+ Control (n=10)

[1]Fudim M et al., Effects of Atrioventricular Interval Modulation Therapy in Subjects with Hypertension and Diastolic Dysfunction. JACC: Advances. Vol. 4, No. 7, July 2025:101896. **Definitions:** DD (Diastolic Dysfunction), BL (Baseline), 6M (6 Months), LV (Left Ventricular), NS (Not Significant).

AVIM Therapy has Potential to Lower Blood Pressure & Improve Cardiac Function

HFpEF is Steadily Increasing and Expected to Become the Dominant Heart Failure Phenotype

1 **Hypertension is a key contributor**
To the diastolic dysfunction → HFpEF cascade

2 **AVIM Therapy is a device-based therapy**
with an immediate, substantial, and sustained effect on blood pressure

3 **AVIM Therapy offloads the heart**
reduces preload and afterload, modulates the autonomic nervous system

4 **Favorable hemodynamics**
can lead to reverse remodeling

5 **Infrastructure and workflow**
for implanting and managing device patients exists globally today



Have a Question?

Scan the QR code to submit.