UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): June 11, 2024

ORCHESTRA BIOMED HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-39421**	**92-2038755**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

150 Union Square Drive
New Hope, Pennsylvania 18938
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (215) 862-5797

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.0001 per share	**OBIO**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

A copy of a slide presentation that Orchestra BioMed Holdings, Inc. (the "Company") uses at investor and industry conferences and presentations is attached to this Current Report on Form 8-K ("Current Report") as Exhibit 99.1 and is incorporated herein solely for purposes of this Item 7.01 disclosure.

The information in Item 7.01 of this Current Report, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of such section. The information in Item 7.01 of this Current Report, including Exhibit 99.1, shall not be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any incorporation by reference language in any such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Investor Presentation.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ORCHESTRA BIOMED HOLDINGS, INC.

By: /s/ Andrew Taylor
Name: Andrew Taylor
Title: Chief Financial Officer

Date: June 11, 2024


Orchestra BioMed
Orchestra BioMed
AVIM Therapy R&D DAY
June 11, 2024
Bringing medical innovation to life

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.

Agenda and Speakers

Agenda

- Introduction and Orchestra BioMed Overview, David Hochman
- Unmet Hypertension Treatment Need in Older High-Risk Patients, David Kandzari, M.D.
- Evidence Supporting AVIM Therapy Mechanism of Action, Vivek Reddy, M.D.
- Clinical Data from the MODERATO I and II Studies, Vivek Reddy, M.D.
- Rationale and Design of the BACKBEAT Global Pivotal Study, David Kandzari, M.D.
- Closing Remarks and Q&A, David Hochman

Presenters

David Hochman
CEO, Chairman, Founder
Orchestra BioMed

David Kandzari, M.D.
BACKBEAT Study Co-PI,
Piedmont Heart Institute

Vivek Reddy, M.D.
BACKBEAT Study Advisor,
Mount Sinai Hospital

Q&A

Darren Sherman
COO, President, Founder
Orchestra BioMed

Avi Fischer, M.D.
SVP, Medical Affairs and Innovation
Orchestra BioMed

Orchestra BioMed Overview

David Hochman

Chief Executive Officer, Founder
Chairman, Orchestra BioMed

Orchestra BioMed Executive Overview

Partnership-enabled business model designed to:

Accelerate innovation to patients & yield exceptional future profitability

Lead Program

Atrioventricular Interval Modulation (AVIM) Therapy

- **Targets >$10B** annual hypertension markets
- Statistically significant efficacy data from double-blind, randomized pilot study
- BACKBEAT global pivotal study ***now enrolling***

Strategic collaboration

Medtronic

Double-digit revenue share

Pipeline Program

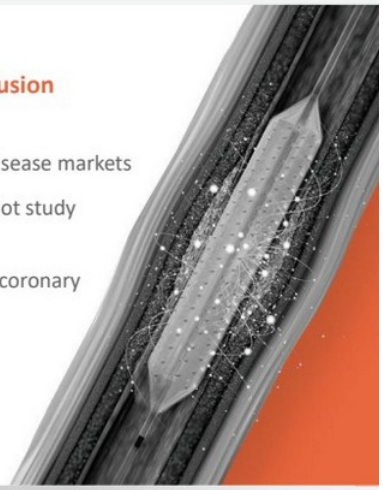
Virtue® Sirolimus AngioInfusion Balloon (SAB)

- **Targets >$4B** annual artery disease markets
- Strong 3-year multi-center pilot study efficacy data
- Conditional IDE approved for coronary pivotal study

Strategic collaboration

TERUMO

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

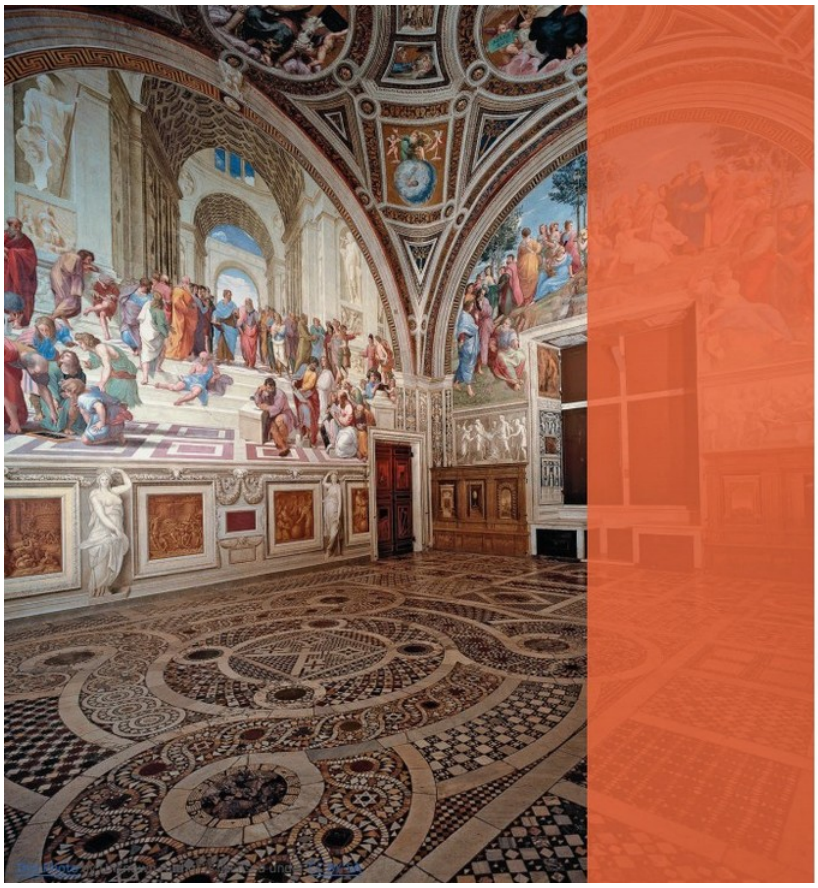
Shared Benefits
Innovation

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

Strategic Partners
Commercialization

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

Orchestra BioMed



A Renaissance is Happening Now…

Renaissance (n):

A **revival or renewed interest** in something; learning from the past to create something better for the future

- Art
- Architecture
- Science
- **Music**
- **Device innovation?**

Orchestra BioMed

The Renaissance of Orchestra

orchḗstra

Ancient Greece: the circular space in front of the stage where ***the chorus performed***

Orchestra

Renaissance Italy: a group of musicians performing a composition with pre-specified instrumentation

The chorus in Classical Greek drama was a group of actors who *described and commented upon the main action of a play with song, dance, and recitation*

Claudio Monteverdi (1567-1643)

The "Father" of the Symphony Orchestra

In order for his music to be replicated ***exactly*** as he composed it; he required it be played with specific instrumentation:

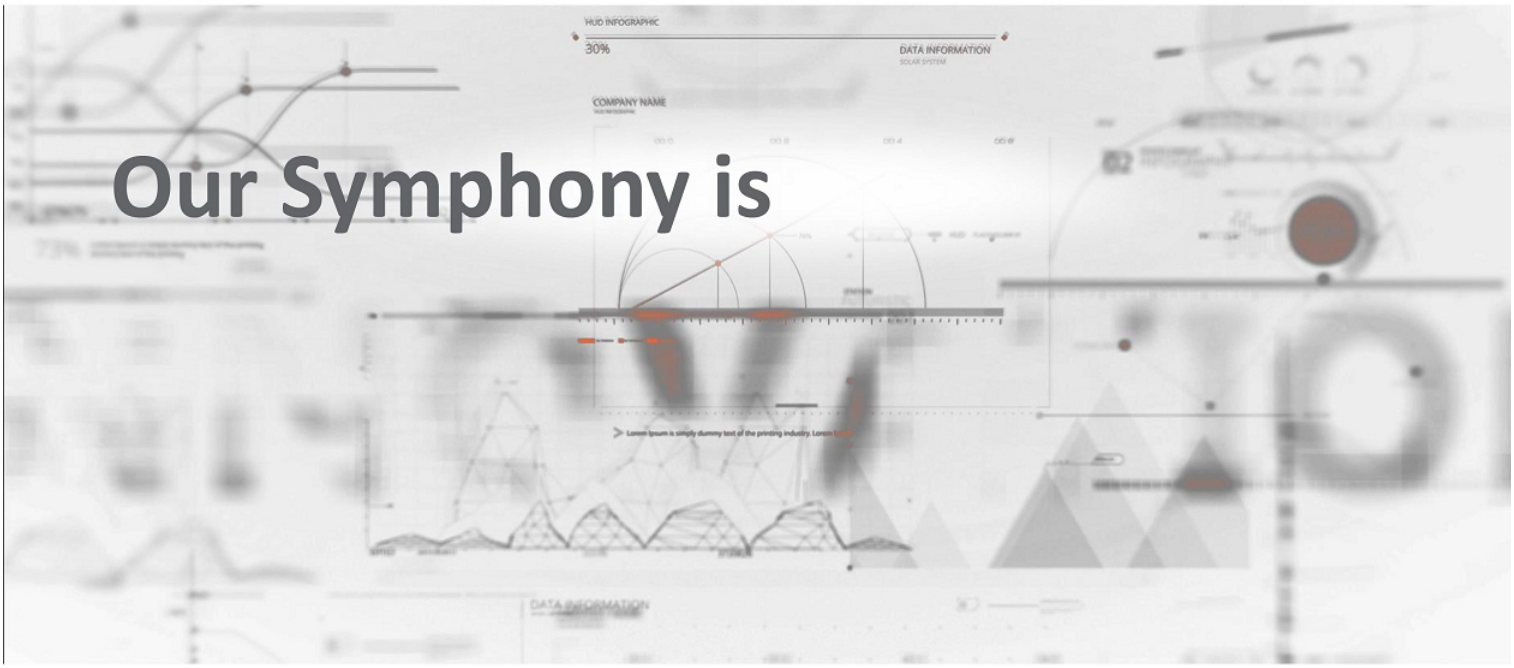
15 viols of different sizes; 2 violins; 4 flutes, 2 large and 2 medium; 2 oboes, 2 cornetts, 4 trumpets, 5 trombones, a harp, 2 harpsichords, and 3 small organs.

*"In the history of Western musical tradition, the evolution of **symphony orchestra** to its modern form can be seen as an apotheosis of instrumental music."*

An Orchestra Succeeds Through 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



Our Symphony is

The Current Renaissance in Cardiac Pacing and Balloon Angioplasty

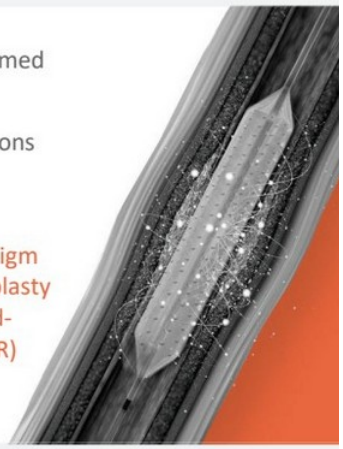
Our large, established target markets, built on foundational technologies introduced 50+ years ago, are experiencing a *RENAISSANCE*, enhancing the opportunity for our innovative technologies

AVIM Therapy

- 1st pacemaker implanted in **1958** by Senning
- Leadless and conduction system pacing opening potential for expanded clinical use
- **AVIM therapy** driving potential use of pacemakers for treatment of **hypertension** and possible expanded indications

Virtue® SAB

- 1st balloon angioplasty performed in **1977** by Grüntzig
- Drug-coated angioplasty balloons are becoming the preferred treatment for artery disease
- **Virtue SAB** expands the paradigm as the only non-coated angioplasty balloon that delivers extended-release sirolimus (SirolimusEFR)



Orchestra BioMed

AVIM Therapy Strategic Collaboration with Medtronic

Orchestra BioMed™

- Developed BackBeat CNT (AVIM therapy) from concept stage; owns all related IP
- Conducted all prior development and the MODERATO I & II clinical studies
- Partnered with Medtronic for global regulatory approval and commercialization
- Sponsor for the BACKBEAT Global Pivotal Study
- **$500 - $1,600 revenue share** per AVIM-enabled device assuming existing reimbursement structures[1]

Medtronic

- Global market leader in cardiac pacing therapy: **>$1.5B in annual revenues**
- Pivotal trial utilizing premium commercial devices
- Providing clinical & regulatory resources
- 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.

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
- Leverages existing reimbursement structures

- 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

The Unmet Treatment Need for Hypertension in Older High-Risk Patients

David Kandzari, M.D., FACC, FSCAI
Chief, Piedmont Heart Institute and Cardiovascular Services
Chief Scientific Officer, Piedmont Healthcare
Director, Interventional Cardiology, Piedmont Heart Institute
Co-principal investigator of the BACKBEAT Study

Hypertension is a Common and Serious Global Health Problem[1]

Hypertension (HTN) is the **leading risk factor for death globally**, and a significant portion of U.S. adults with HTN remain uncontrolled

~120 million (48%) of U.S. adults have HTN

~25 million (21%) are prescribed only lifestyle modification

~95 million (79%) are prescribed lifestyle modification and medication

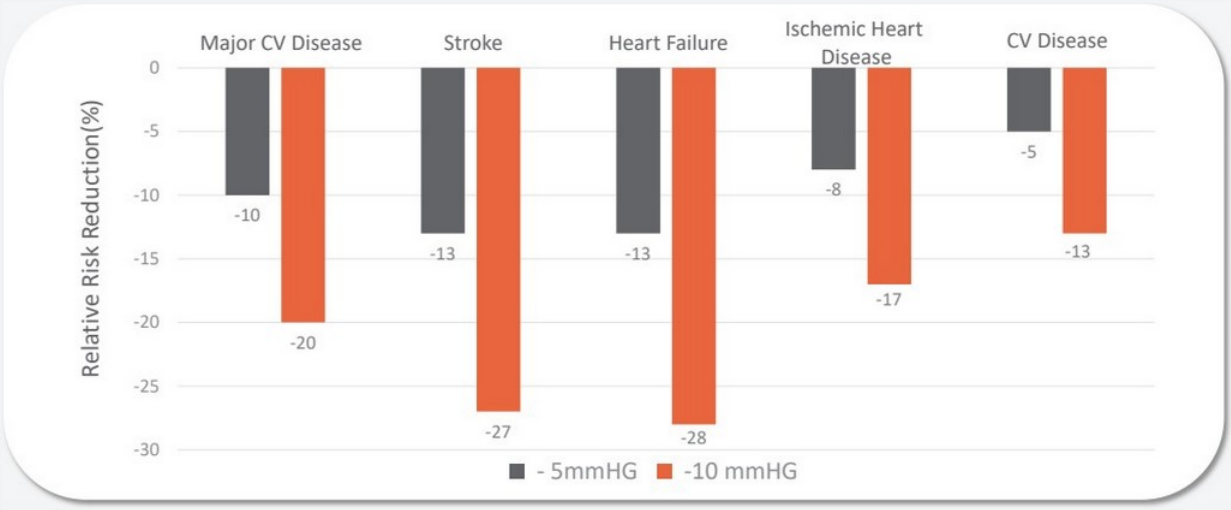
~93 million (78%) remain uncontrolled

[1]Hypertension Cascade: Hypertension Prevalence, Treatment and Control Estimates Among US Adults Aged 18 Years and Older Applying the Criteria From the American College of Cardiology and American Heart Association's 2017 Hypertension Guideline—NHANES 2017–2020. CDC. May 12, 2023. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html.

Orchestra BioMed

Modest Reductions in Blood Pressure (BP) Have Significant Clinical Benefit

Reductions as low as 5mmHg in office systolic blood pressure (oSBP)
substantially decrease the Relative Risk (%) of common cardiovascular conditions



[1] Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2021;397(10285):1625-36.
[2]Ettehad D, et al. *Lancet*. 2016;387(10022):957-67.

Challenges with Pharmacotherapy for Hypertension

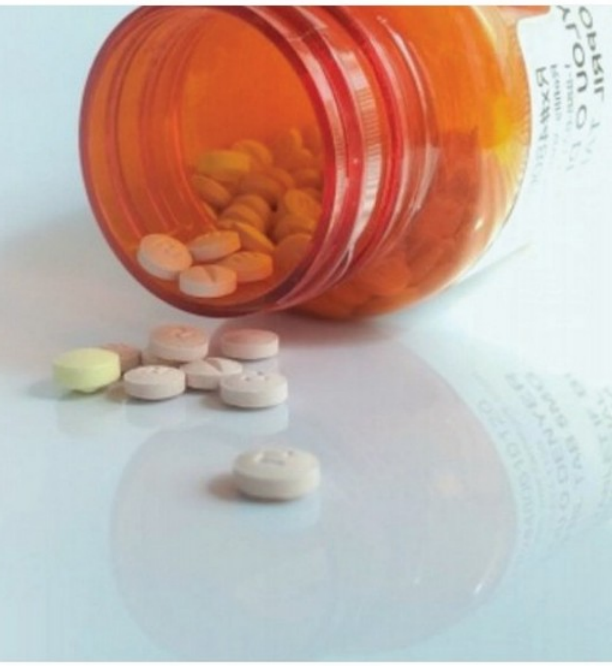
While pharmacologic therapy is often effective, many patients experience insufficient BP control[1]

Patient compliance is particularly difficult in HTN

- HTN is the “silent killer,” and most patients are asymptomatic
- Medications often have significant side effectsthat feel worse than the disease itself
- ~50% of patients adhere to prescribed medications

Many pharmacotherapies provide insufficient BP control

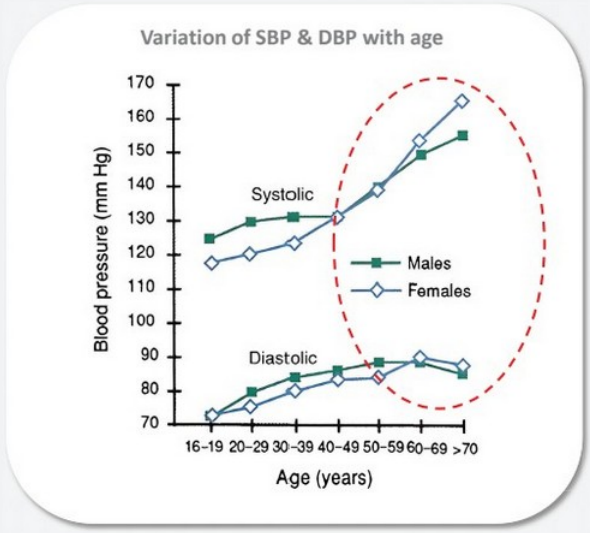
- > 40% of HTN patients remain uncontrolled despite pharmacotherapy
- Isolated systolic hypertension (ISH), emerges as the predominant form of HTN as patients age

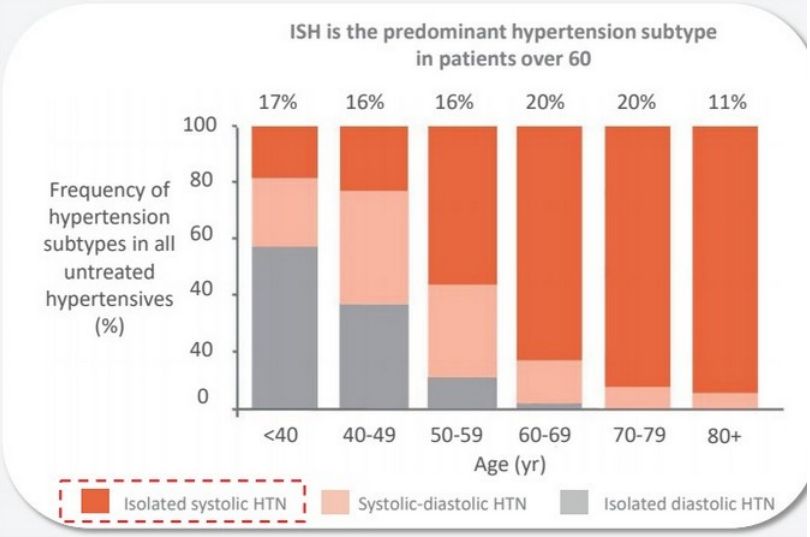


[1]Burnier M, et al., Adherence in hypertension. *Circ Res*. 2019 Mar;124(7): Whelton et al., 1124-1140; 2018https://doi.org/10.1161/CIR.0000000000000596Circulation. 2018;138:e484–e594

The Nature of Hypertension Changes with Age

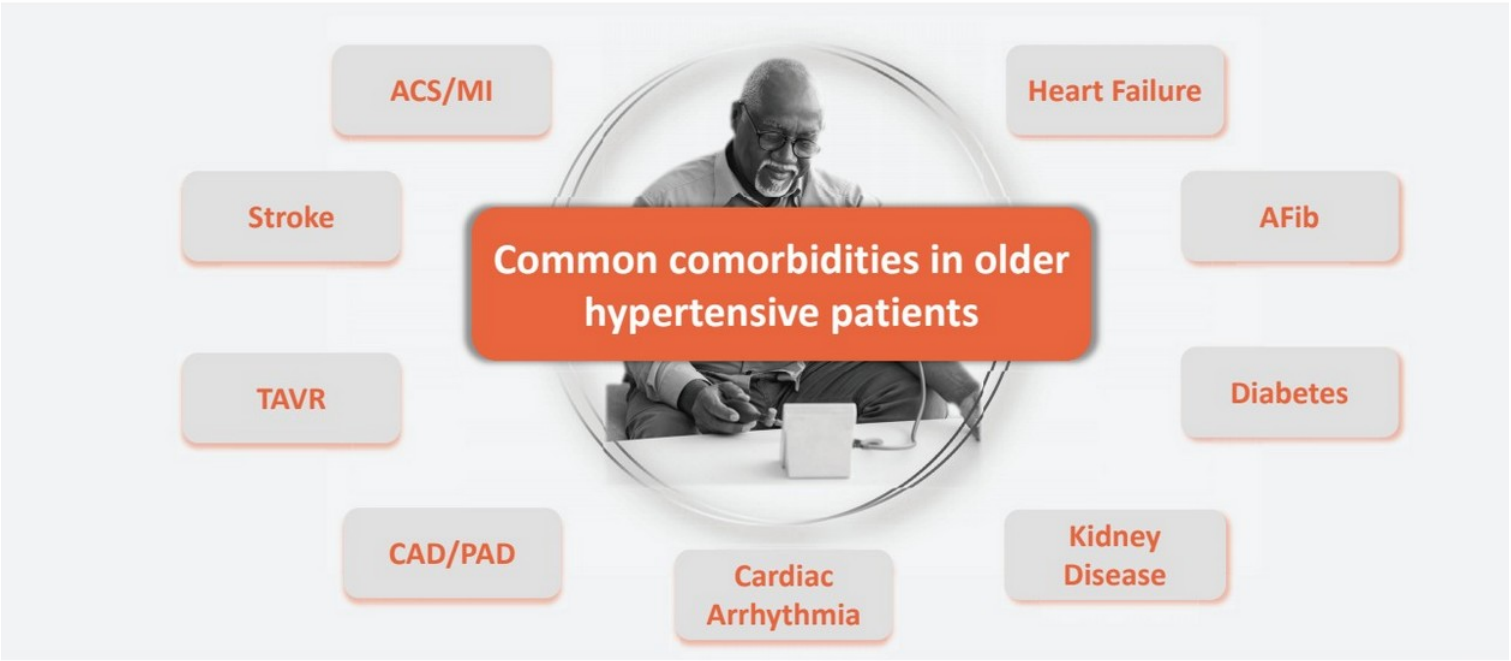
Due to arterial stiffening, older patients have higher prevalence of ISH leading to substantially greater risk of CV complications (CAD, CHF, stroke, mortality)[1]





[1]Lilly L, 2021, Wolters Kluwer; Franklin SS, *J Clin Hypertens*. 2006;8:444-449; ***Definitions***: NHANES: National Health and Nutrition Examination Survey; CAD: Coronary Artery Disease; CHF: Coronary Heart Failure

Older Patients with Hypertension Frequently Have Significant Comorbidities[1]



[1]Company estimates based on published sources; **Definitions**: Acute coronary syndrome (ACS); myocardial infarction (MI); transcatheter aortic valve replacement (TAVR); coronary artery disease (CAD); peripheral artery disease (PAD); atrial fibrillation (Afib)

Hypertensive Patients with Pacemakers: An Older, Higher Risk Population in Need of Better Treatment Options[1]

73 years
average age

70% of patients with pacemakers also have HTN

Over **750K new HTN + PPM patients annually worldwide**

Frequent additional comorbidities: **atherosclerosis, hyperlipidemia, diabetes mellitus, and chronic kidney disease**

More likely to have ISH – a type of HTN for which there are **limited therapeutic options**

[1]Company estimates based on published sources; **Definition**: Permanent pacemaker (PPM)

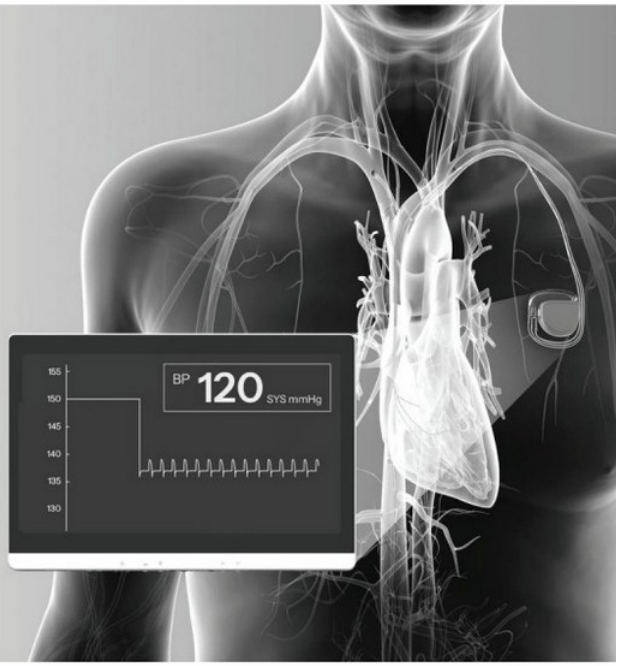
Orchestra BioMed

Compelling Opportunity to Evaluate AVIM Therapy

BACKBEAT IDE Pivotal study: currently enrolling

- Evaluating a novel investigational hypertension therapy that takes advantage of existing pacemaker
- Same device implant and treating physicians
- No additional daily compliance requirements for patients

Pilot study data show AVIM therapy drives **robust reduction in 24-hr aSBP in high-risk patient population with high rates of ISH, HFpEF, and other comorbidities**



Definitions: Heart failure with preserved ejection fraction (HFpEF)

Orchestra BioMed

Evidence in Support of AVIM Therapy Mechanism of Action

Vivek Reddy, M.D.

Director, Cardiac Arrhythmia Services at Mount Sinai Hospital

Director, Electrophysiology at Mount Sinai Health System

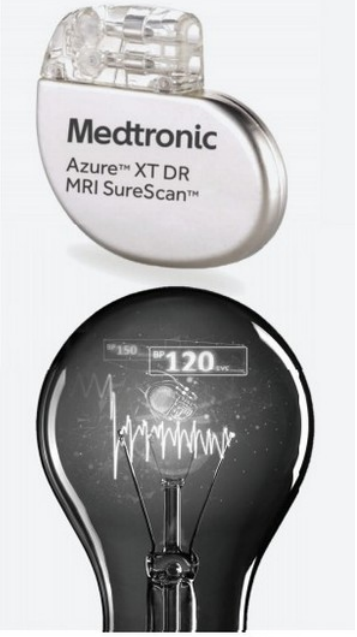
Professor of Medicine, The Icahn School of Medicine at Mount Sinai

BACKBEAT Study Clinical Steering Committee Member

Orchestra BioMed

AVIM Therapy Summary*

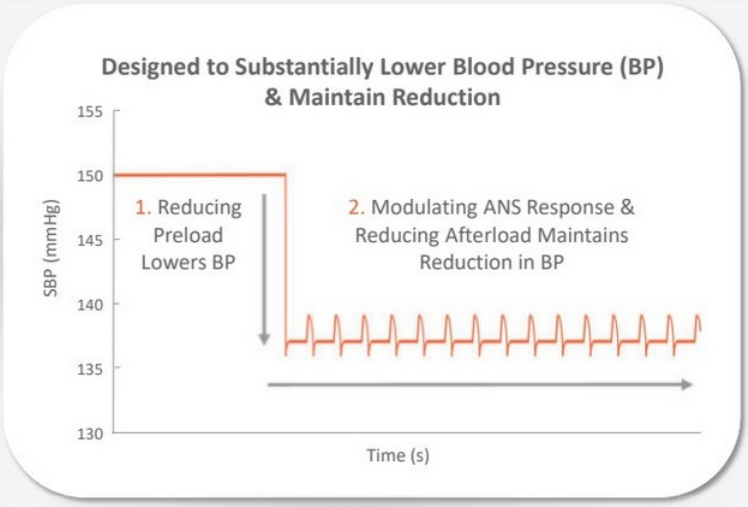
- Programmable and adjustable device-based HTN therapy designed to be delivered via dual-chamber pacemaker
  - Integrated for use with Medtronic Astra™ or Azure™ MRI-compatible pacemakers
  - Leverages previously completed or already indicated procedure
  - Can be activated, adjusted or deactivated, as needed
- Compatible with conduction system pacing (CSP) or right ventricular (RV) lead placement
- Data from previous preliminary clinical studies demonstrate an immediate, substantial, & persistent effect in reducing blood pressure



*AVIM therapy is investigational and not commercially approved. No claims can be made until regulatory approvals.

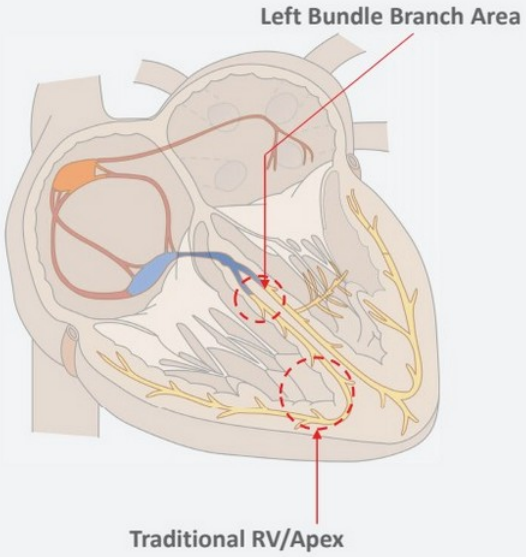
Novel AVIM Therapy Mechanism of Action Designed to Substantially and Persistently Reduce Blood Pressure

- AVIM therapy uses a dual-chamber pacemaker to deliver programmed sequences of **short AV intervals** interspersed with **longer AV intervals** designed to reduce blood pressure by:
  - Reducing cardiac preload
  - Modulating autonomic nervous system (ANS) response
  - Reducing afterload
- Designed to utilize well characterized physiologic mechanisms, including the Frank-Starling law, to **improve circulatory hemodynamics**:
  - Reduced intra-cardiac volumes and pressures
  - Improved cardiovascular efficiency
  - No adverse impact on contractility
- Compatible with **conduction system pacing (CSP)** lead placements or traditional pacing lead locations



Emerging Role of Conduction System Pacing in Cardiac Pacing Therapy

- Cardiac rhythm market **rapidly adopting CSP** via left bundle branch area pacing (LBBAP)
- LBBAP is a pacing approach that **taps into the heart's natural electrical system**, helping ensure pacing closely mimics physiologic contractions, **allowing the ventricles to work in coordination**
- Clinical data demonstrate **AVIM compatibility with CSP**

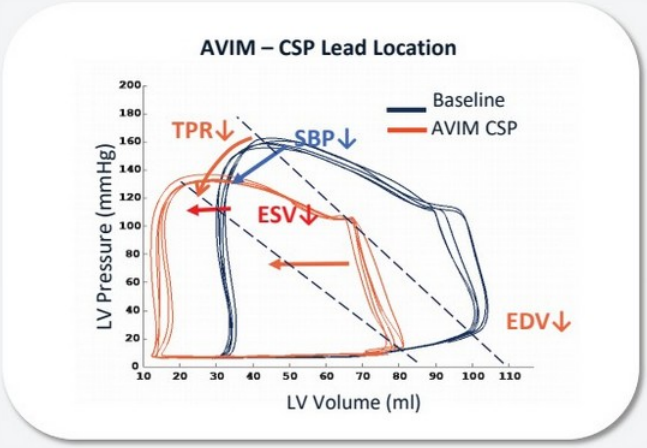


Invasive Pressure Volume (PV) Loop Study Shows Favorable Acute Hemodynamics from AVIM Therapy[1]

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

Decreases total peripheral resistance
(↓ TPR)

Decreases systolic blood pressure
(↓ SBP)

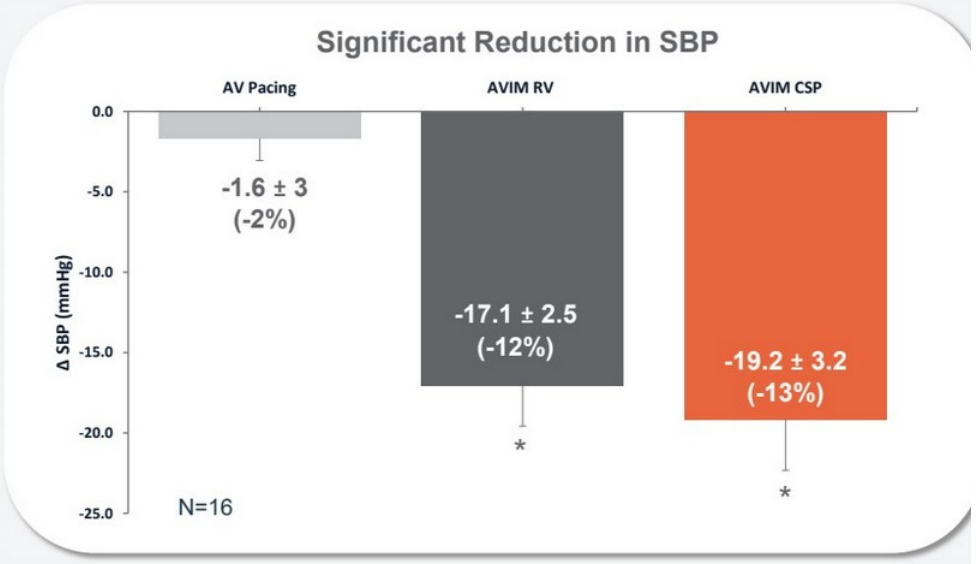


- N = 16 subjects indicated for a pacemaker with uncontrolled hypertension despite medical therapy
- Paired data (baseline vs. AV Sequential pacing or baseline vs. AVIM) reported

Data on file with Orchestra BioMed. [1]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24.
Definitions: EDV (end-diastolic volume), ESV (end-systolic volume), LVP (left ventricular pressure).

AVIM Therapy Reduces Systolic Blood Pressure[1]

Significant reduction in SBP with AVIM therapy and **no significant difference between right ventricular (RV) and conduction system pacing (CSP)** lead placement

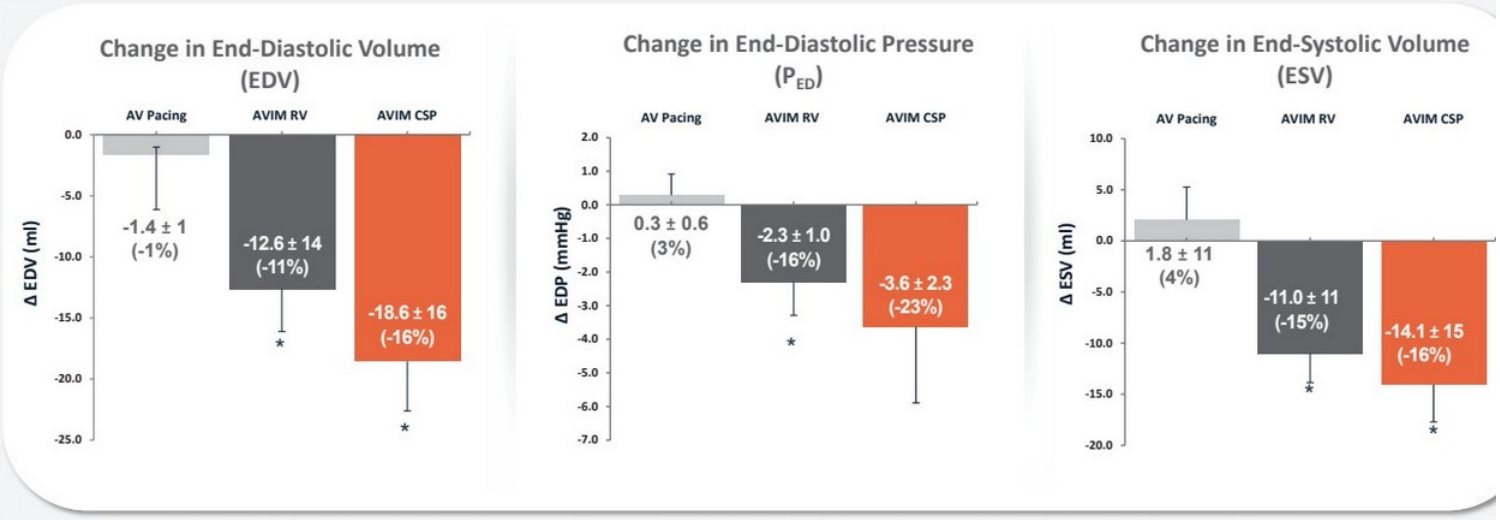


*P < 0.05 (compared to baseline); no significant difference between AVIM RV & AVIM CSP

[1]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24.

AVIM Therapy has a Favorable Impact on Cardiac Hemodynamics[1]

Significant reductions in EDV, P_{ED} & ESV



N=16

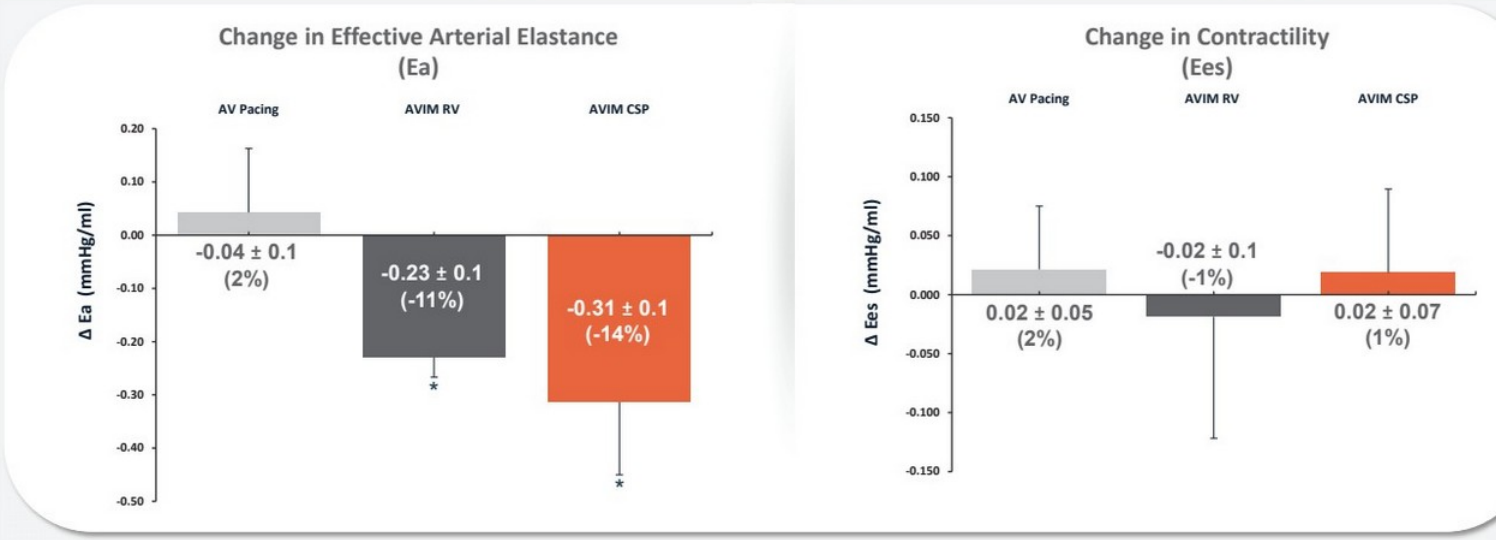
*P < 0.05 (compared to baseline); no significant difference between AVIM RV & AVIM CSP

[1]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24.

Orchestra BioMed

AVIM Therapy has a Favorable Impact on Cardiac Hemodynamics[1]

Reduction in total peripheral resistance (Ea) & no change in contractility (Ees)

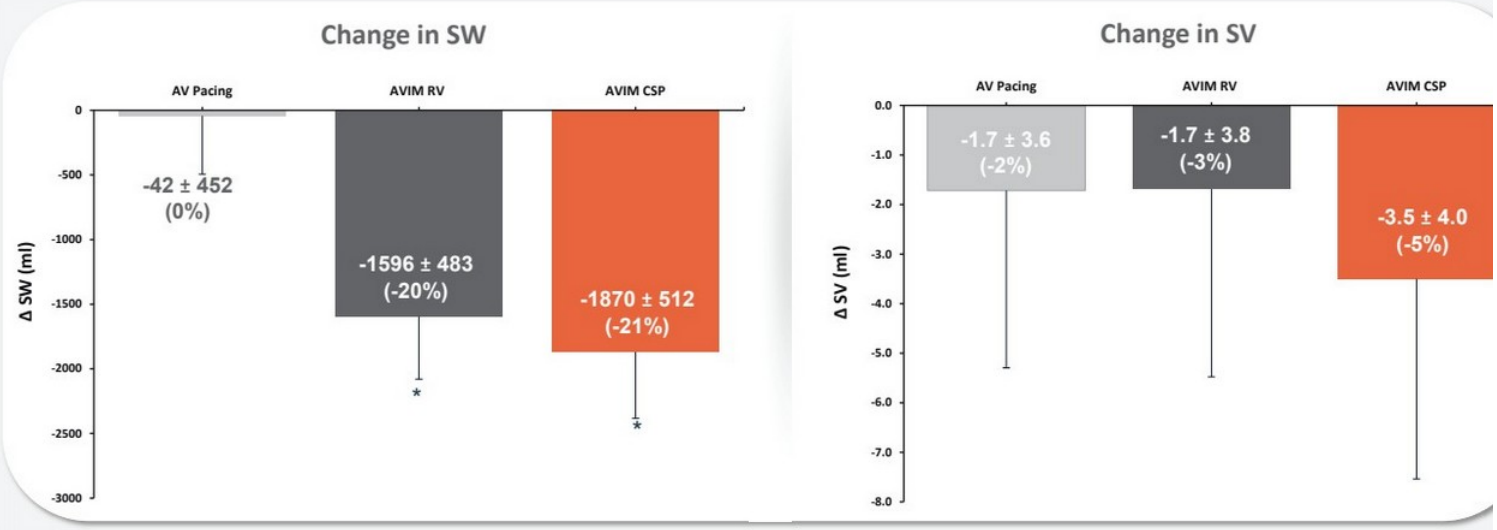


N=16 *P < 0.05 (compared to baseline); no significant difference between AVIM RV & AVIM CSP

[1]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24;
Definitions: Ea (arterial elastance) (Ees (end-systolic elastance, which is a measure of contractility)

AVIM Therapy has a Favorable Impact on Cardiac Hemodynamics[1]

Significant reduction in stroke work (SW) without significant reduction in stroke volume (SV)



N=16

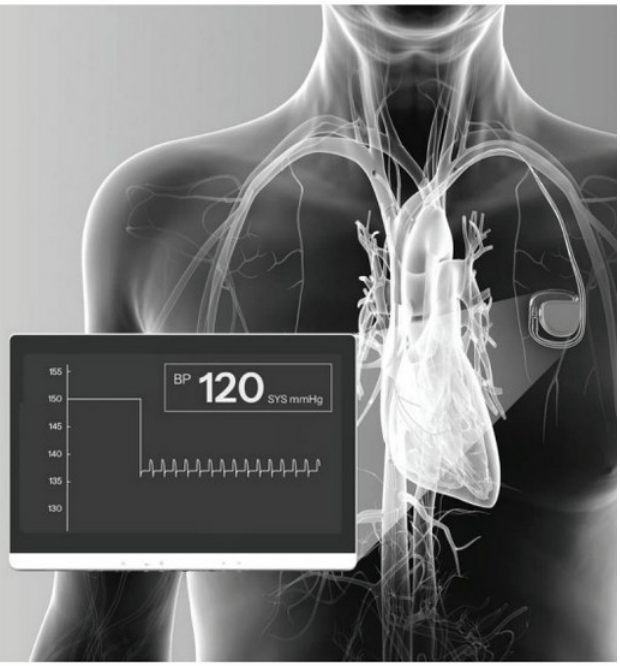
*P < 0.05 (compared to baseline); no significant difference between AVIM RV & AVIM CSP

[1]Kuck, Hemodynamics Effects of AVIM Therapy, THT'24.

Orchestra BioMed

AVIM Mechanism of Action Highlights

- AVIM therapy is designed to use a dual-chamber pacemaker to deliver programmed sequences of **short AV intervals interspersed with longer AV intervals to reduce blood pressure**
- Preliminary data support the mechanism of action and **demonstrated a favorable impact of AVIM therapy on cardiac hemodynamics**, independent of RV pacing lead location



Clinical Data

MODERATO I & II Pilot Studies

Vivek Reddy, M.D.

Director, Cardiac Arrhythmia Services at Mount Sinai Hospital

Director, Electrophysiology at Mount Sinai Health System

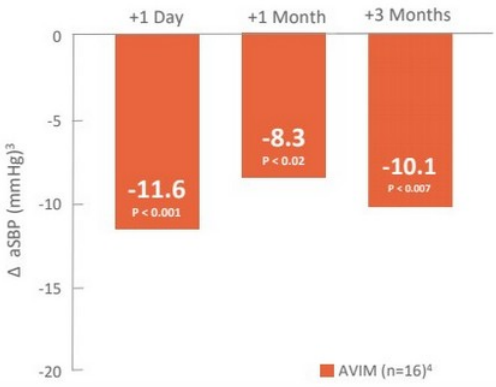
Professor of Medicine, The Icahn School of Medicine at Mount Sinai

BACKBEAT study Clinical Steering Committee Member

MODERATO I Study Design & Results

- **Prospective, single-arm study** of 27 patients with persistent hypertension (office systolic blood pressure (oSBP) > 150mmHg) despite 2 or more anti-hypertensive medications & an indication for pacemaker
  - 1-month run-in to account for Hawthorne effect, followed by 3 months activation
- Primary safety & efficacy assessed at **3 months post AVIM therapy activation**; follow-up through 2 years[1,2]

Significant Reduction in 24-Hour aSBP



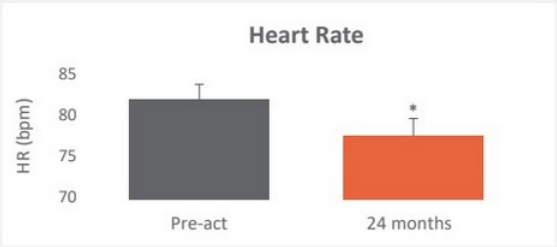
Significant Reduction in oSBP Through 24 Months

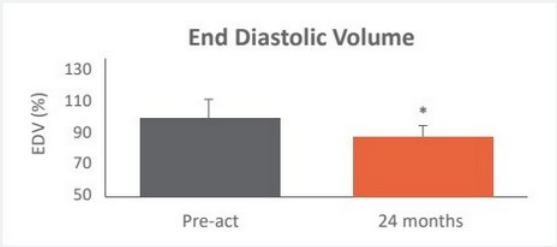
[1]Neuzil et al. *Journal of the Am Heart Assoc*. 2017;6:e006974. https://doi.org/10.1161/JAHA.117.006974. [2]Burkhoff MODERATO I Study 2-Year Results TCT 2018. [3]Compared to pre-activation. [4]aSBP (n=160 at pre-activation. [5]AVIM (n=21) continued after completion of study at 3 months to be followed for 2 years. ***Definitions:***, aSBP (Ambulatory Systolic Blood Pressure).

Orchestra BioMed

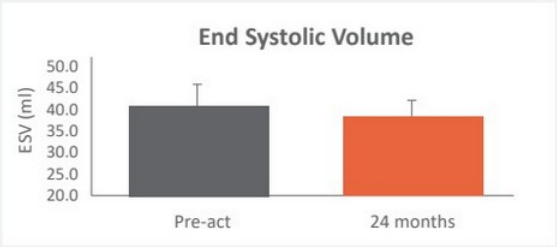
MODERATO I: Safety Data at 24 Months

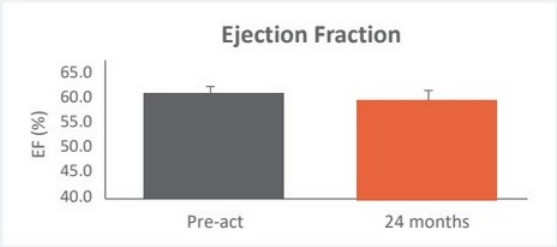
Significant Reduction in End-Diastolic Volume & Heart Rate with No Significant Change in Ejection Fraction (EF





* P<0.05



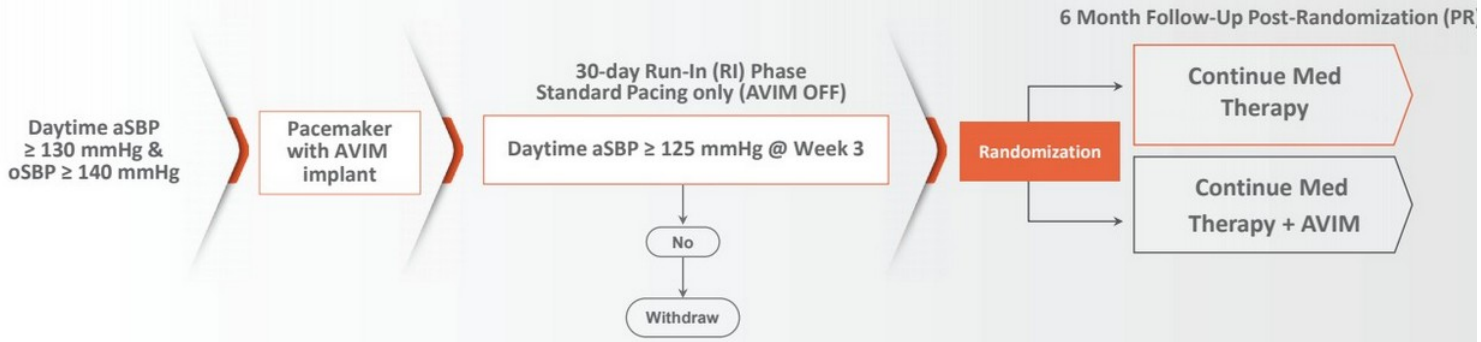


[1]Burkhoff MODERATO I Study 2-Year Results TCT 2018.

MODERATO II Study Design[1]

Prospective, multi-center, double-blind study investigating the efficacy of AVIM therapy in patients with persistent hypertension and an indication for pacemaker

- Primary safety & efficacy assessed at **6 months post AVIM activation**; continued follow-up to 2 years



[1]Burkhoff MODERATO II Study 2-Year Results TCT 2021. **Definitions**: IPG (Implantable Pulse Generator).

MODERATO II: Patient Demographics

No significant differences between groups at baseline

	Control (n=21)	AVIM Therapy (n=26)	p-value
Age	74.9 ± 8.5	73.2± 9.0	0.518
Gender	15 M / 6 F	15 M / 11F	0.375
LVEF (%)	58.4±4.9	59.8±6.3	0.414
Medical History			
Diabetes	9 (42.9%)	12 (46.2%)	0.999
Prior Atrial Fibrillation	6 (28.6%)	5 (19.2%)	0.505
Coronary Artery Disease	9 (42.9%)	10 (38.5%)	0.775
Stroke	0 (0%)	1 (3.8%)	0.999
Medications	3.3±1.4	3.3±1.6	0.886
Isolated Systolic Hypertension	71.4%	88.5%	0.263
24-Hr aSBP	136.3±12.5	136.3±9.2	0.995
24-Hr aDBP	72.6±6.7	74.0±6.9	0.478
Ambulatory Heart Rate (24-hour)	68.4±8.5	69.6±9.5	0.670
oSBP	154.4±15.5	153.1±15.8	0.781
oDBP	81.6±12.4	83.0±10.8	0.693
Office Heart Rate	66.5±10.9	67.1±12.0	0.848

Definitions: LVEF (left ventricular ejection fraction), aDBP (ambulatory diastolic blood pressure), oDBP (office diastolic blood pressure).

MODERATO II Randomized, Double-Blind Results

AVIM therapy showed encouraging results in MODERATO II, a prospective, multi-center, randomized (AVIM therapy + medical therapy vs. continued medical therapy), controlled, double-blind, pilot study of patients with pacemakers and persistent hypertension

Significant Reduction in 24-Hr aSBP and oSBP[1,2]

-11.1 mmHg
in 24-Hour aSBP
at 6 months

0%
MACE vs. 14.3% in control group at 6 months

-17.5 mmHg
in oSBP
at 2 years

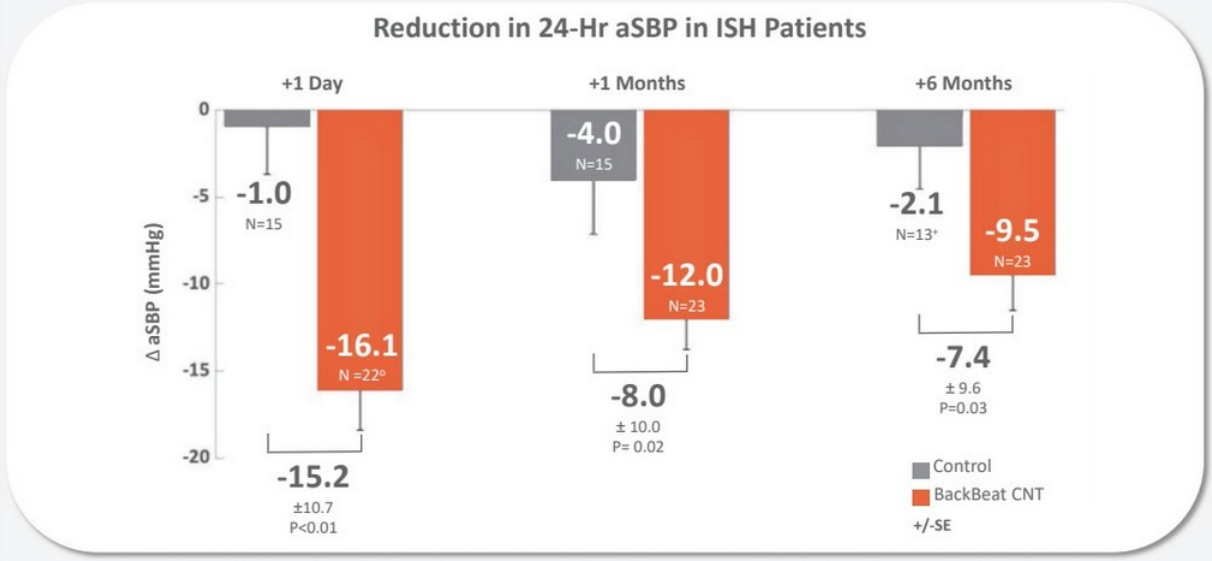
85%
of patients with reduction in aSBP

[1]Kalaras et al. *Journal of the Am Heart Assoc*. 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); **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

MODERATO II: Significant aSBP Reduction in ISH Patients

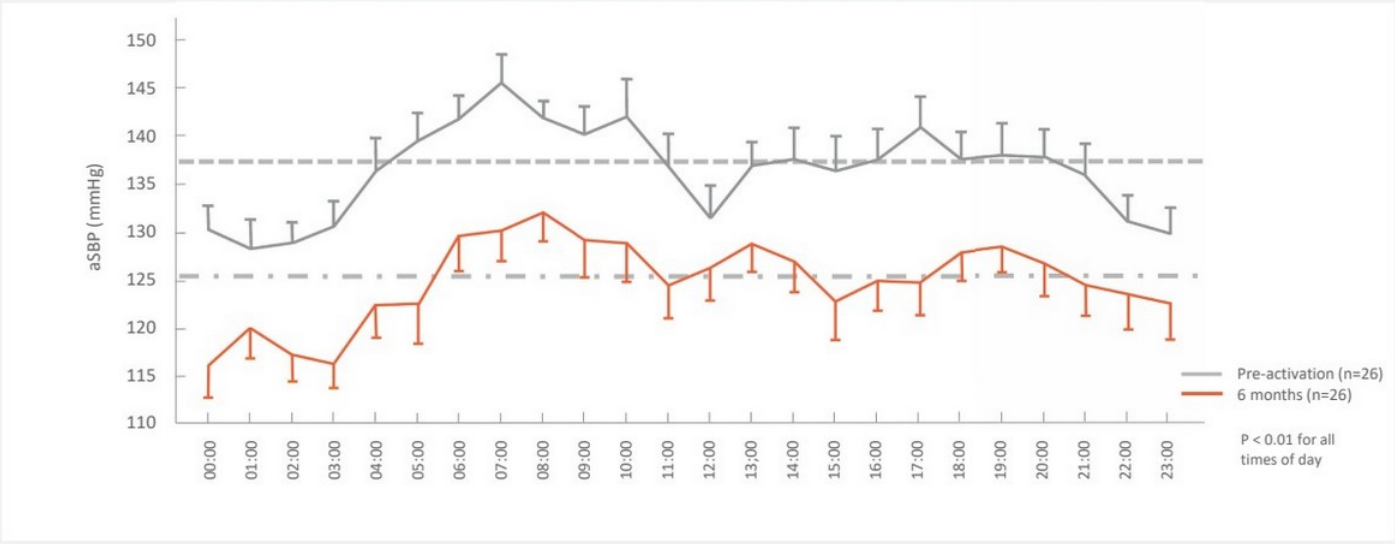
7.4 mmHg reduction in aSBP at 6 Months compared to control



° aSBP could not be measured on 1 patient despite repeat measurement (patient had extremely high blood pressure);
+13 control had data at 6 months, one died of cancer, and one had unsuccessful recording

MODERATO II: Significant Reduction in 24-hour aSBP[1]

Paired average 24-hour aSBP profile after 6 months of AVIM therapy demonstrate reduction in SBP with preservation of normal daily blood pressure variations



[1]Burkhoff MODERATO II Study 2-Year Results TCT 2021.

MODERATO II: High Overall Response Rate to AVIM Therapy[1]

6 Months Post-Randomization

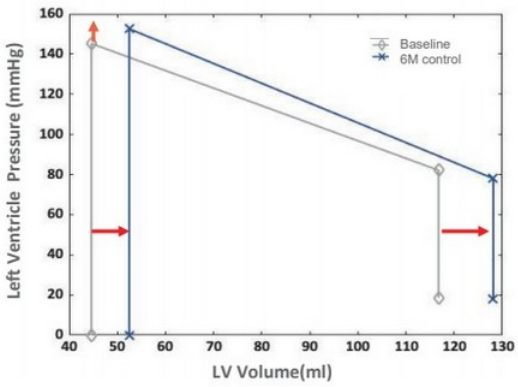
	AVIM (n=26)	Control (n=19)
Isolated Systolic Hypertension (ISH)	**88.5%**	**71.4%**
% with Reduction in aSBP	**85%**	**53%**
% with > 5 mmHg Reduction in aSBP	**65%**	**42%**
% with > 10 mmHg Reduction in aSBP	**54%**	**21%**

[1]Kalarus et al. *Journal of the Am Heart Assoc*. 2021;10:e020492 ahajournals.org/doi/10.1161/JAHA.120.020492.

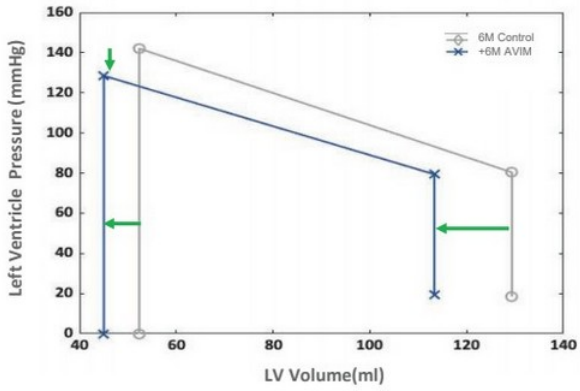
MODERATO II: Chronic, Non-Invasive PV Loop Data Show Favorable Effects on Cardiac Remodeling[1]

AVIM Therapy affects adverse remodeling

Unfavorable remodeling in control patients after 6 months resulted in increases in ESV, EDV, & ESP



Favorable reverse remodeling 6 months after crossover to AVIM therapy demonstrated by reductions in ESV, EDV, & ESP[2]



[1]Paired data (N=12, N=6); [2]6 months of control followed by 6 months of AVIM therapy after crossover (12 months from baseline). **Definition**: ESP (End-Systolic Pressure)

MODERATO II: Long-Term SBP Reduction with AVIM Therapy

AVIM therapy demonstrated sustained, long-term reduction in 24-Hr aSBP

Long-term blood pressure from a follow-up study of 16 patients from MODERATO II*

- 8 AVIM & 8 control patients who crossed-over to AVIM therapy at the end of the 6-month double-blind phase of MODERATO II & agreed to be followed long-term
- Each patient had aSBP and oSBP measured at an average of **3.6 years** (±0.6) following initiation of AVIM therapy

*Patients were re-consented for long-term follow-up

Significant Reduction in 24-Hr aSBP and oSBP[1,2,3]

P-value between 6 months & 3.6 years (±0.6) = non-significant

-8.9 mmHg in 24-Hour aSBP from baseline at **3.6 years** (±0.6)

-12.5 mmHg in oSBP at **3.6 years** (±0.6)

100% of patients with reduction in aSBP at **3.6 years** (±0.6)

[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]Fischer MODERATO Study Long-term Results ICI 2024;

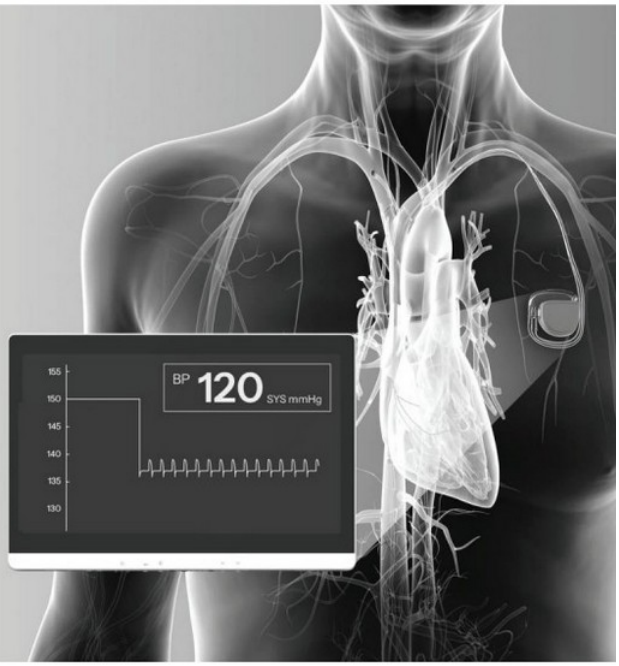
Orchestra BioMed

AVIM Clinical Results Summary

AVIM therapy resulted in:

- **Significant reduction in mean aSBP & oSBP at 6 months, in a group where 88.5% were ISH patients**
  - 85% overall response rate to treatment with AVIM therapy
  - 54% experiencing > 10mmHg reduction in aSBP at 6 months
- Significant reduction in oSBP & aSBP **maintained through 3.6 years**
- **Low overall MACE** with no difference between groups

Chronic PV loop data support the mechanism of action and demonstrate a **favorable impact of AVIM therapy on cardiac hemodynamics**



Rationale and Design of the BACKBEAT Global Pivotal Study

David Kandzari, M.D., FACC, FSCAI

Chief, Piedmont Heart Institute and Cardiovascular Services

Chief Scientific Officer, Piedmont Healthcare

Director, Interventional Cardiology, Piedmont Heart Institute

Co-principal investigator for the BACKBEAT Study

BACKBEAT STUDY

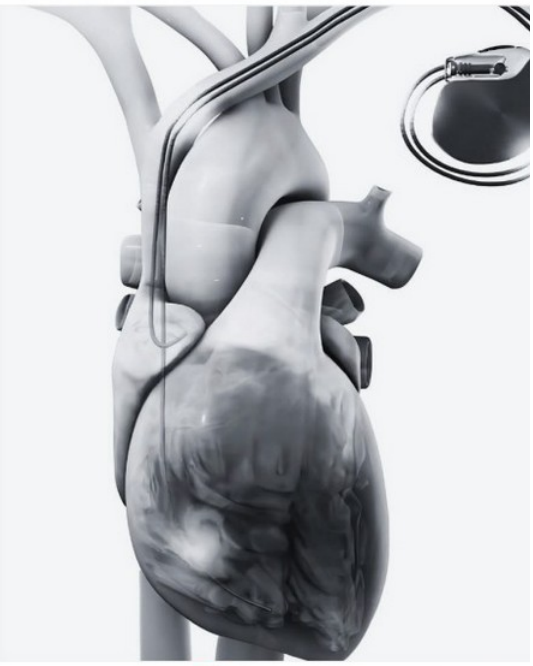
Orchestra BioMed

Novel Design for a Device-Based Therapy

BACKBEAT
GLOBAL PIVOTAL STUDY

Global, pivotal randomized, controlled, double-blind study in which all patients:

- Receive Medtronic dual-chamber pacemaker implant
- Have the investigational RAMware downloaded to their device
- Undergo follow-up testing with AVIM therapy ON and OFF
- Are managed by a blinded study team



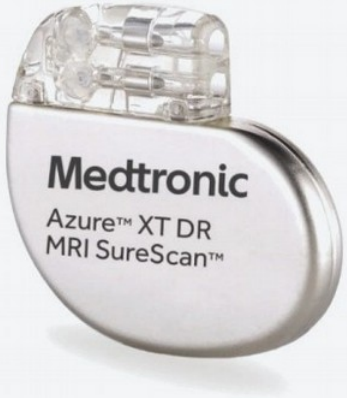
BACKBEAT GLOBAL PIVOTAL STUDY Orchestra BioMed

BACKBEAT Study Target Population

Patients Indicated for a Dual-Chamber Pacemaker Who Also Have Uncontrolled Hypertension Despite Use of Antihypertensive Medications

Eligibility: recently received *de novo* implant of a dual-chamber pacemaker system (including leads)

- All patients are indicated for a dual-chamber pacemaker
- Sinus node dysfunction & AV block patients are eligible
- Favorable risk/benefit profile with procedure independent of study
- Workflow & implant technique do not change
  - Leads can be placed in CSP or traditional RV locations



BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Clinical Steering Committee Members

Co-Principal Investigators

Andrea M Russo
Electrophysiology

David Kandzari
Interv. Cardiology, HTN

Steering Committee Members

Vivek Reddy
Electrophysiology

Béla Merkely
Electrophysiology

Charles Love
Electrophysiology

Felix Mahfoud
Interv. Cardiology, HTN

JoAnn Lindenfeld
Advanced Heart Failure

Raymond Townsend
Nephrology

Definitions: Interv (Interventional)

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Approximately 50% of Patients Will be Enrolled Outside of the US

Study will randomize approximately **500 patients across ~80 study sites**

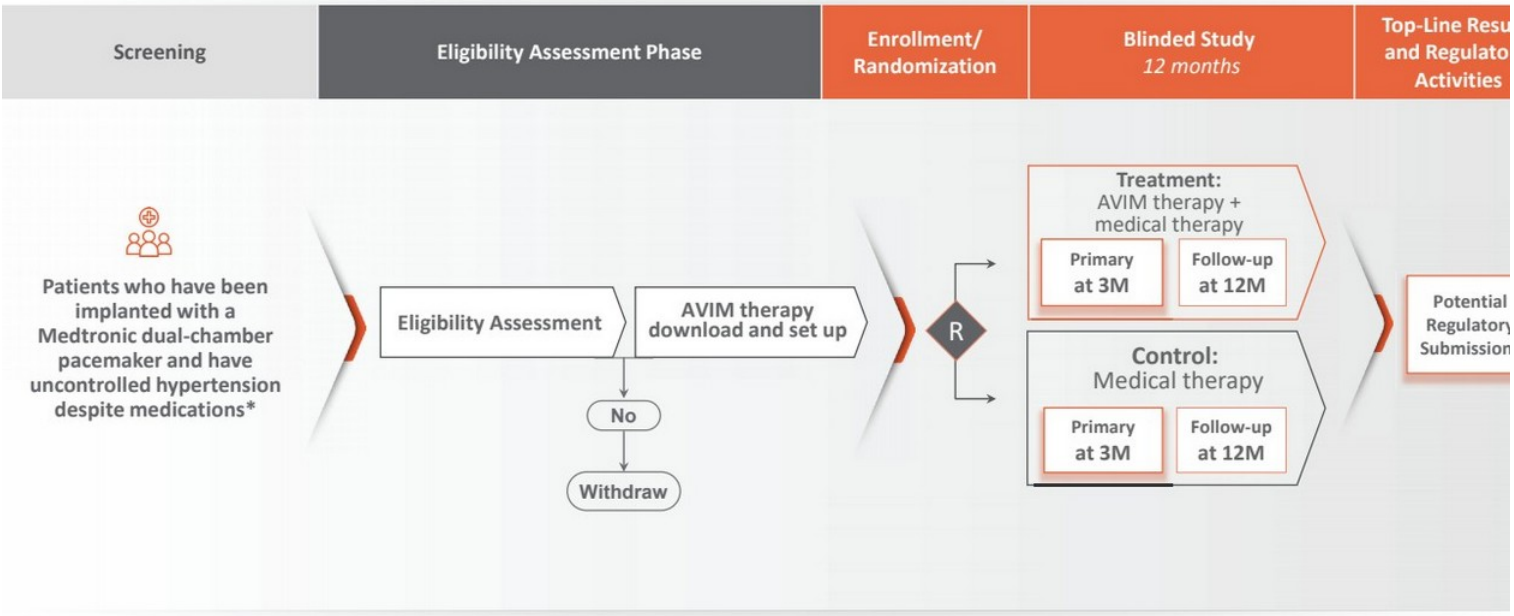
Participating countries include:

- Belgium
- Czech Republic
- Germany
- Hungary
- Poland
- Spain
- Switzerland
- The Netherlands
- UK
- US

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

BACKBEAT Study Design



*Implant is decoupled from study outcomes & endpoints.

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Key Inclusion and Exclusion Criteria

Inclusion

- Recently received a **Medtronic Astra/Azure dual chamber pacemaker**
- On a stable anti-HTN treatment regimen of **1, 2 or 3 classes of anti-HTN drugs**
- oSBP **≥ 140 mmHg and < 180 mmHg**
- Average 24-Hour aSBP **≥ 130 mmHg and < 170 mmHg**

Exclusion

- Presence of conditions that **limit effective delivery of AVIM therapy** (i.e., permanent or significant atrial fibrillation, severe valvular disease)
- **Left ventricular (LV) dysfunction** (reduced ejection fraction) and/or **symptomatic heart failure (HF)**
- Recent cardiovascular procedures, renal denervation, other active implantable devices and significant kidney impairment

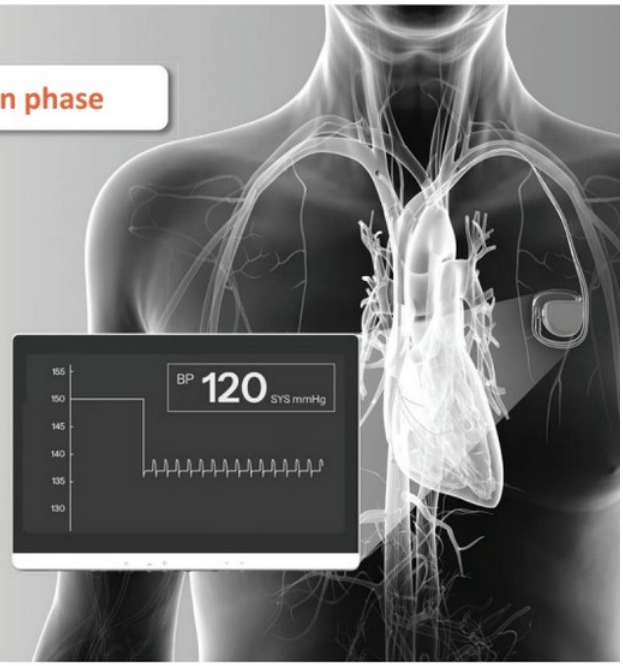
BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Set-Up Procedure Determines Enrollment and Randomization

≥ 5 mmHg reduction is required to proceed to randomization phase

- **AVIM RAMware downloaded** onto previously implanted pacemaker **in all patients**
- Response to AVIM therapy activation assessed acutely:
  - Observe blood pressure reduction
  - Determine stability of reduction
  - Optimize therapy parameters for each patient



Orchestra BioMed

Double Blind Phase: Primary Endpoints

Primary Efficacy Endpoint:

Between group difference in the **change of mean 24-hour ambulatory systolic blood pressure (aSBP) at 3 months** post-randomization

- aSBP is the gold-standard measurement of blood pressure
- 3 months is the standard duration to demonstrate efficacy in HTN studies
- Balances time needed to demonstrate efficacy with ability to maintain medication regimens

Primary Safety Endpoint

Freedom from **unanticipated serious adverse device events at 3 months** post-randomization

- Potential complications of pacemaker implant & follow-up are well-established
- Aims to identify unique & unexpected adverse events **directly related to AVIM therapy (treatment group only)**

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Double-Blind Follow-up Through 12-Months to Collect Additional Data

Hypertension

Between-group difference in:

- Mean Change of 24-hour aSBP immediately after randomization
- Mean change in 24-hour ambulatory pulse pressure (aPP)
- Mean reduction of oSBP at 3 months post-randomization

Adverse Events

Between group comparison:

- Freedom from the composite cardiovascular adverse events (CCAE) rate 12 months post-randomization
  - Including mortality, stroke, MI, HF, AFib, HTN crisis, decline in eGFR

Medications

Between group comparison:

- Reduction in anti-hypertensive medication burden at 3-months
  - Medication dose, number, and/or class

Definition: Estimated glomerular filtration rate (eGFR)

BACKBEAT GLOBAL PIVOTAL STUDY

Orchestra BioMed

Key Takeaways and Q&A

Key Takeaways

- **Hypertension is the leading risk factor for death** & most common comorbidity in patients with pacemakers globally
- AVIM therapy is an investigational, **programmable & adjustable treatment** developed by Orchestra BioMed
- AVIM therapy is designed to have an **immediate, substantial, & persistent effect in reducing blood pressure**
- Invasive PV loop studies support the mechanism of action and **demonstrate a favorable impact of AVIM therapy on cardiac hemodynamics, when pacing from traditional RV lead locations or left bundle branch area**
- Data from the MODERATO I & II studies demonstrated a **favorable efficacy and safety profile**
- BACKBEAT global pivotal study is being conducted in **collaboration with Medtronic, the global leader in cardiac pacing therapy**

Q&A

Moderator

David Hochman
CEO, Chairman, Founder
Orchestra BioMed

Darren Sherman
COO, President, Founder
Orchestra BioMed

Avi Fischer, M.D.
SVP, Medical Affairs
and Innovation
Orchestra BioMed

David Kandzari, M.D.
BACKBEAT Study Co-PI,
Piedmont Heart Institute

Vivek Reddy, M.D.
BACKBEAT Study Advisor,
Mount Sinai Hospital