# Orchestra BioMed


**BACKBEAT Study Overview:**

**B**radyc**A**rdia pa**C**ema**K**er with AV interval modulation for **B**lood pr**E**ssure tre**A**tmen**T**

*September 2023*

# Forward-Looking Statements

*Certain statements included in this press release 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 initiation and design of the BACKBEAT pivotal study, the FDA's approval of the BACKBEAT pivotal study, the Company providing additional information to the FDA and the Company's late-stage development programs, strategic partnerships and plans to expand its product pipeline. These statements are based on various assumptions, whether or not identified in this press release, 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 quarterly report on Form 10-Q filed with the U.S. Securities and Exchange Commission on May 12, 2023, 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 press release. The Company does not plan and undertakes no obligation to update any of the forward-looking statements made herein, except as required by law.*



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# AVIM Therapy Overview

Strategic collaboration with Medtronic

***Atrioventricular Interval Modulation (AVIM)*** *therapy (also known as* ***BackBeat CNT™****) is designed to immediately, persistently and substantially reduce blood pressure*

## Unmet Need

- Hypertension is the **leading global risk factor for death**
- Hypertension is also the **#1 comorbidity in the pacemaker population (over 70%)**[1]
- Older population at **increased risk for major cardiovascular events** & challenges with drug compliance

## Innovation

- Bioelectronic therapy **designed to immediately, persistently and substantially lower blood pressure**
- Seamlessly integrated into existing Medtronic dual-chamber pacemakers
- **Compelling clinical data** from two pilot studies, including a randomized double-blind study

## Initial Opportunity

- **Same target patient population** that already needs a pacemaker
- **Same implant procedure** and large **trained physician pool**
- Leverages **existing pacemaker reimbursement**



[1]Company estimates based on published sources, including National Inpatient Survey (NIS) and National Health and Nutrition Examination Survey (NHANES)

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# Ideal Collaboration

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

***AVIM Therapy:***

*Patented investigational bioelectronic treatment for hypertension*

Medtronic

- Global market leader in cardiac pacing therapy: **>$1.5B** in annual revenues
- Providing leading device plus clinical & regulatory resources
- Exclusive global commercial rights for AVIM therapy in pacemaker-indicated patients
- Right of first negotiation to expand global rights for the treatment of non-pacemaker HTN patients
- **$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**


**>$10 Billion** Potential Annual Global Market Opportunity*

**>3.1M Addressable HTN Patients**

**High Risk HTN** (Non-pacemaker) - Older patients with isolated systolic hypertension (ISH) and other comorbidities

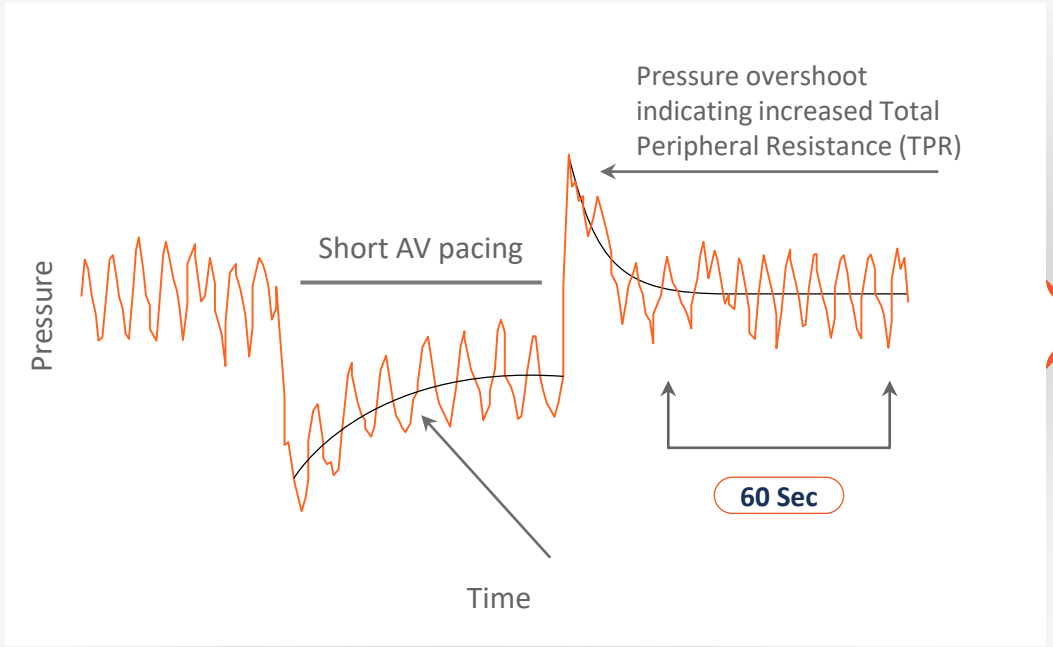
Medtronic is the global leader in pacemakers



*Total addressable market in 2025 based on company estimates; 1Company estimates based on published sources, including National Inpatient Survey (NIS) and National Health and Nutrition Examination Survey (NHANES); Definition: Hypertension (HTN)

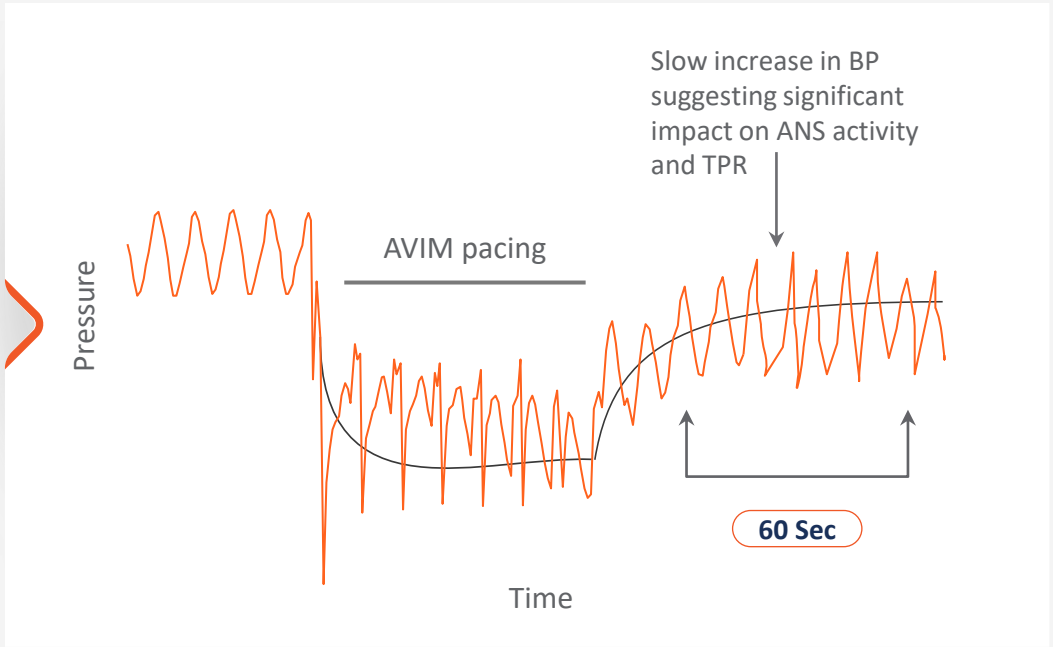
# Novel Mechanism of Action Designed to Substantially Reduce Blood Pressure

Bioelectronic Control of Ventricular Filling Immediately **Reduces Blood Pressure**




**AVIM** ACTIVATION

AVIM-Mediated Pressure Patterns **Modulate Autonomic Nervous System (ANS) Response**






AV (Atrioventricular), TPR (Total Peripheral Resistance)

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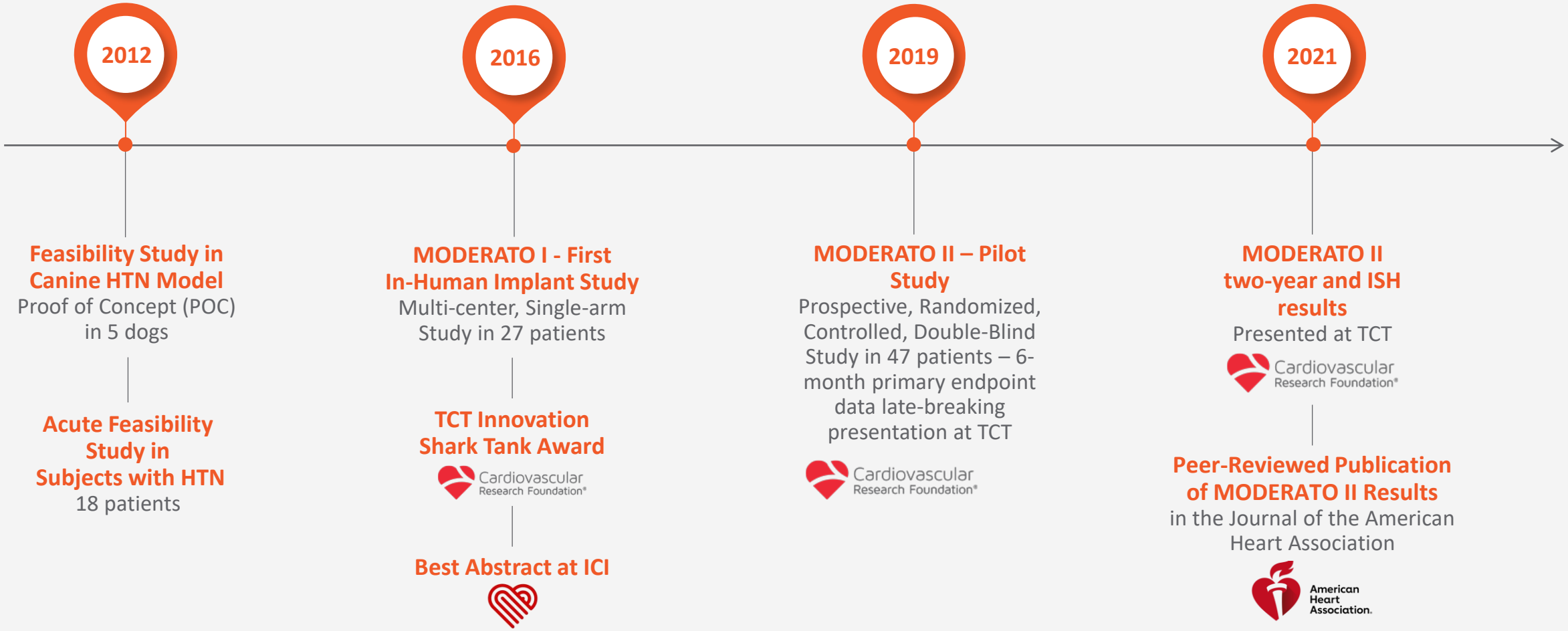
# Existing Body of Clinical Data Supporting Efficacy and Safety



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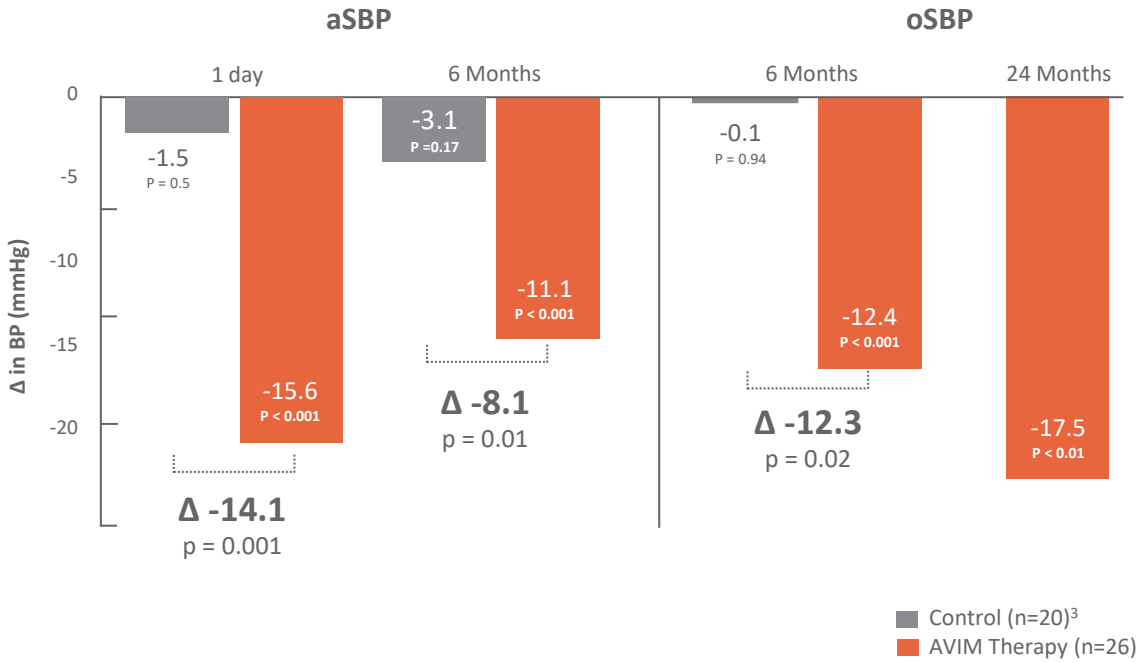
# MODERATO II Randomized, Double-Blind Results

**BackBeat CNT™**
showed encouraging results in MODERATO II, a prospective, multi-center, randomized, (BackBeat CNT + Medical Therapy vs. Continued Medical Therapy), double-blind, pilot study of pacemaker patients with 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. 9.5% 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 American Heart Association. 2021;10:e020492 ahajournals.org/doi/10.1161/JAHA.120.020492; [2]Burkhoff MODERATO II Study 2-Year Results TCT 2021; [3]24-Hr aSBP Control (n=19),1 control patient could not be measured despite repeat measurement (patient had extremely high blood pressure); 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, Office Systolic Blood Pressure (oSBP); Ambulatory Systolic Blood Pressure (aSBP)

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# BACKBEAT Study Summary

Prospective, multi-center, double-blind study investigating the efficacy and safety of AVIM therapy in patients indicated for a dual-chamber pacemaker who also have uncontrolled hypertension (HTN) despite the use of antihypertensive medications

Randomize approximately **500 patients across ~80 study sites** globally

Inclusion and exclusion criteria apply learnings from MODERATO II and other recent HTN clinical studies

Study endpoints:

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



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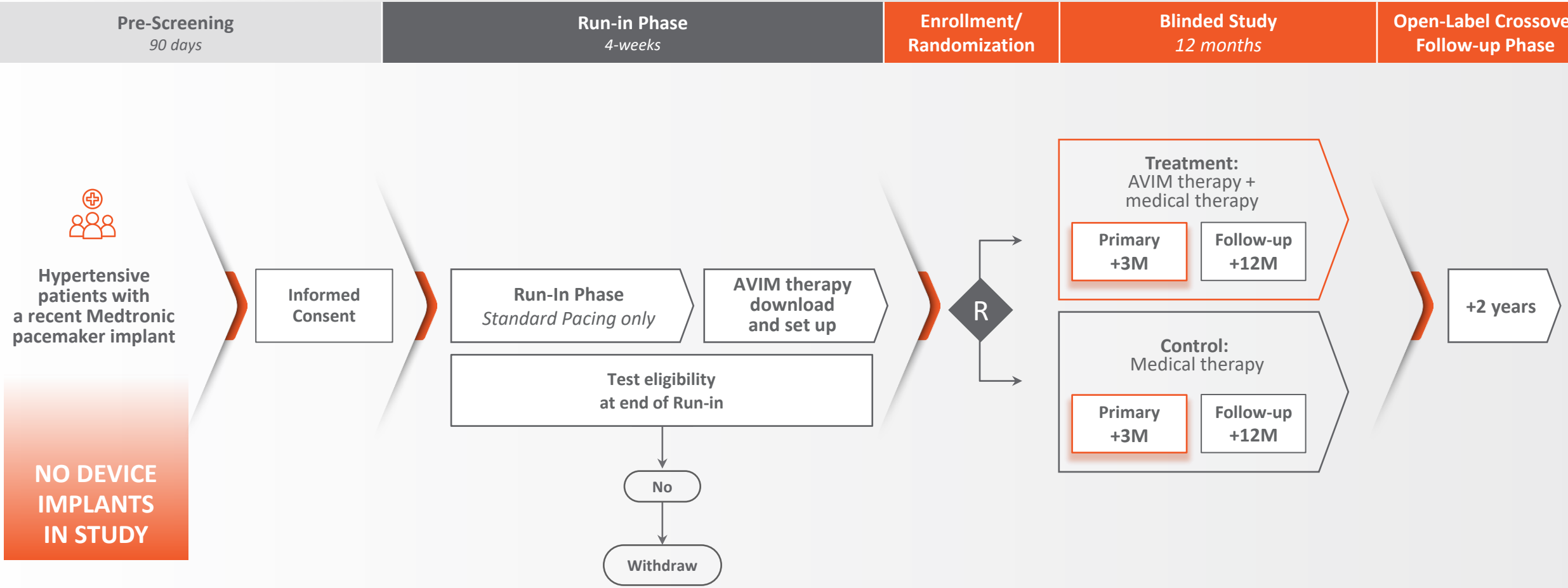
# BACKBEAT Study Design



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# Key Takeaways

- Hypertension is the leading global risk factor for death and #1 comorbidity in pacemaker patients
- Large established pacemaker market and implanting physician community, as well as existing reimbursement
- Patient population with favorable risk-benefit profile as they already require a pacemaker and additional therapy provided by same device offers potential for substantial blood pressure reduction
- MODERATO pilot studies demonstrate immediate, substantial and persistent blood pressure reduction in combination with background medical therapy
- BACKBEAT study robustly powered to generate data in support of potential regulatory approval and commercialization
- Medtronic is the ideal collaborator as the global market leader in cardiac pacing therapy