BackBeat® Cardiac Neuromodulation Therapy (CNT) for Immediate, Substantial and Sustained Lowering of Blood Pressure

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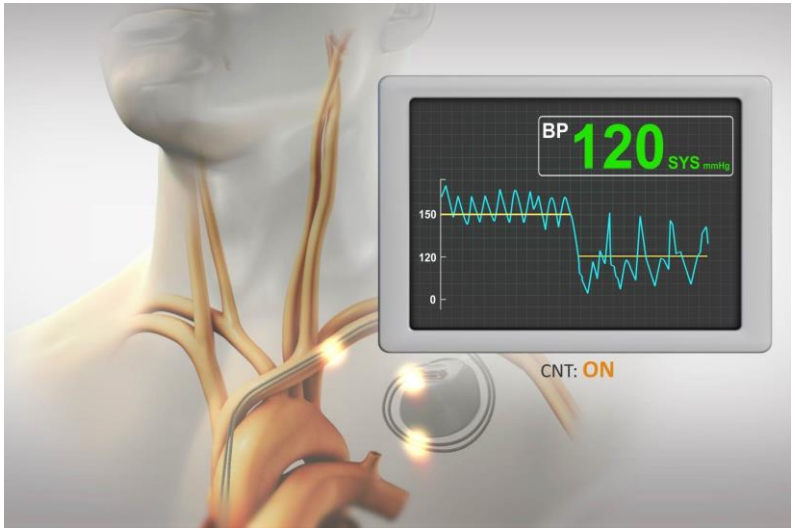
Disclosure Statement of Financial Interest

I, Daniel Burkhoff, MD PHD have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

AFFILIATION/FINANCIAL RELATIONSHIP	*COMPANY*
• *Consultant*	• *BackBeat Medical*/Orchestra BioMed, Inc

BackBeat® Cardiac Neuromodulation Therapy (CNT) Overview

- Bioelectronic therapy that immediately, substantially and chronically lowers blood pressure (BP) while simultaneously modulating Autonomic Nervous System (ANS)
  - Mimics effects of multiple medications by reducing preload, afterload and sympathetic tone
- Can be delivered using standard rhythm management device hardware (such as dual chamber pacemakers)
- Applicable to wide range of hypertensive patients including Isolated Systolic Hypertension
  - Hypertensive patients who are also indicated for a pacemaker
    - Over 70% of pacemaker patients have hypertension
  - Uncontrolled hypertensive patients

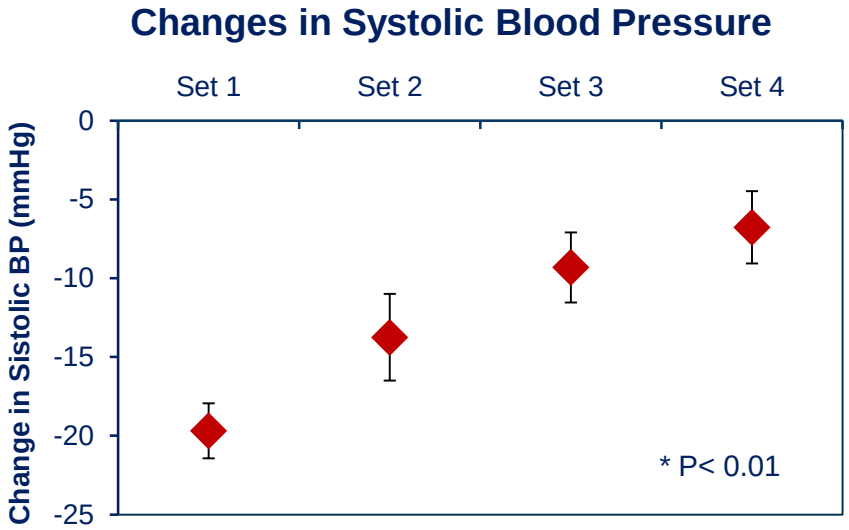


BackBeat® CNT Clinical Benefits

- Programmable: Blood Pressure reduction is adjustable
- Immediate response
- Substantial reduction in Blood Pressure
- Sustained effect
- High responder rate
- Broad applicability
  - All subgroups including ISH
  - Wide range of initial blood pressure
  - Pacemaker and non-pacemaker population

BackBeat® CNT is Programmable and Adjustable

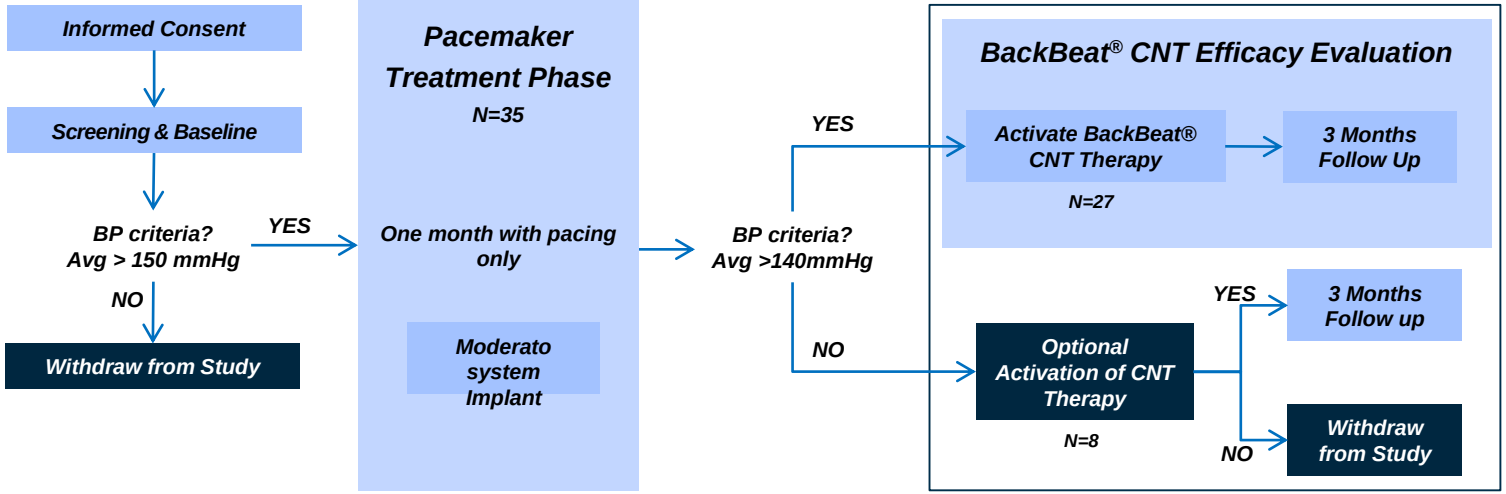
Reduction in Blood Pressure Can be Titrated by Modifying Therapy Parameters as Needed



- **Acute clinical study (N=18) treated with 4 different sets of BackBeat® CNT parameters demonstrates control of the reduction in blood pressure**

BackBeat® CNT MODERATO I Study Design

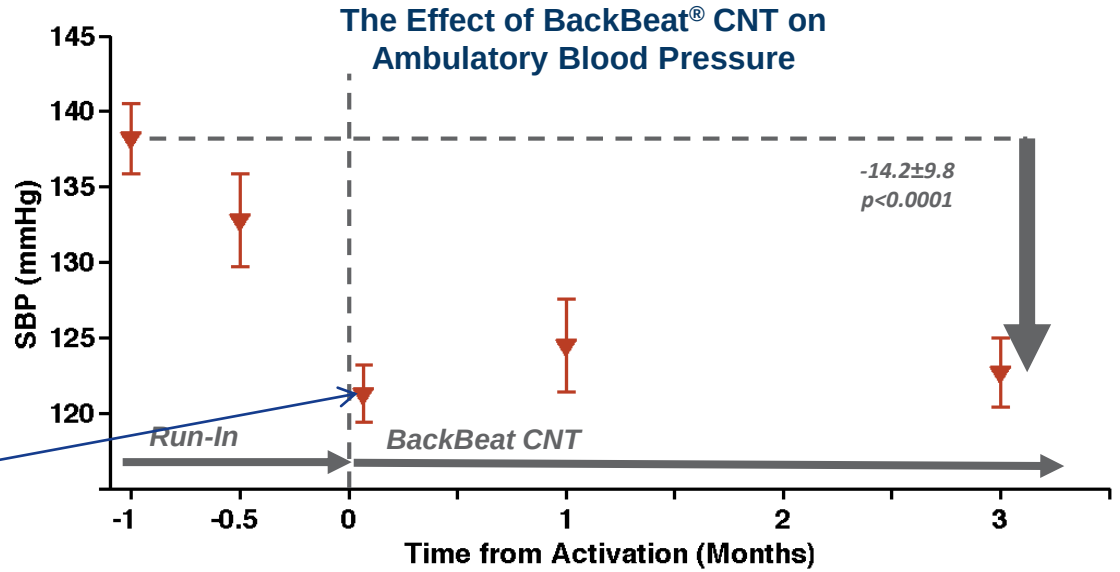
- Patients with Persistent Hypertension (office BP > 150mmHg) despite 2 or more anti-hypertensive medications and an indication for a Pacemaker
- One-month pacemaker only run-in phase
- Primary safety and efficacy evaluation at 3 months post BackBeat® CNT activation; follow-up to 2 years



Immediate & Substantial Reduction in BP

Ambulatory Blood Pressure Decreased Significantly Immediately After Activation and Remained Lowered by 14.2 mmHg After 3 Months of Therapy

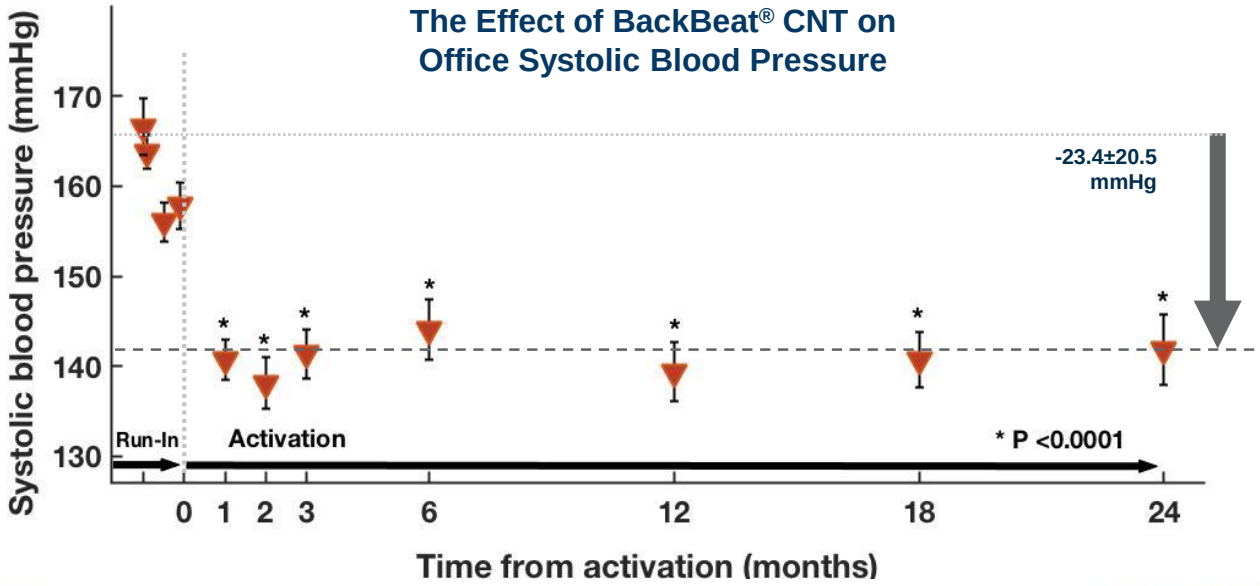
Immediate and Substantial Effect of BackBeat® CNT on Ambulatory Blood Pressure



Petr Neuzil, et. al. Pacemaker-Mediated Programmable Hypertension Control Therapy. J Am Heart Assoc. 2017; Dec 23;6(12): e006974. DOI: 10.1161/JAHA.117.006974

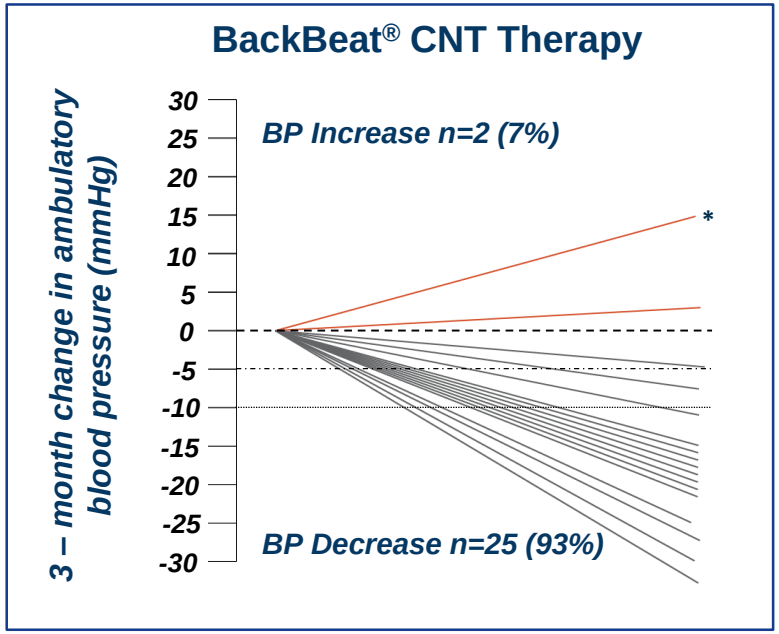
BP Reduction Sustained Through 2 Years

BackBeat® CNT Maintains Significant Reduction in Office Systolic BP over 2 years



High Responder Rate in Challenging Patient Population

- Baseline AMB systolic pressure: 137 mmHg
- Average reduction of 14.2 mmHg
- 78% of patients had Isolated Systolic Hypertension (ISH)
- Responder Rate:
  - 85% SBP reduced > 5mmHg
  - 74% SBP reduced > 10mmHg



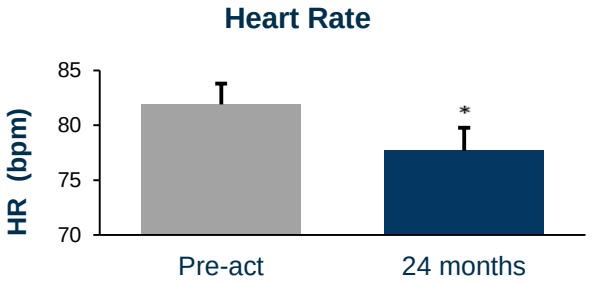
* Patient 76 YO on 5 HTN drugs, non responder to RDN therapy (baseline office BP 168/80); After re-optimization of stimulation parameters 24H AMB BP reduced by 14.3 mmHg and office BP by 33/9 mmHg

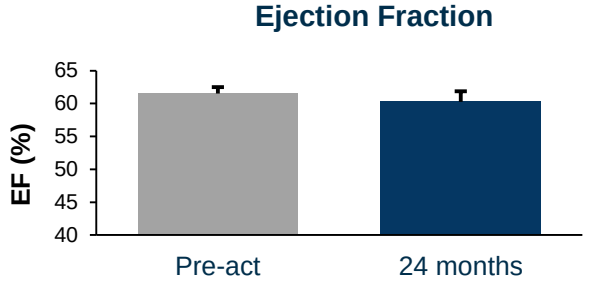
Petr Neuzil, et. al. Pacemaker-Mediated Programmable Hypertension Control Therapy. J Am Heart Assoc. 2017; Dec 23;6(12): e006974. DOI: 10.1161/JAHA.117.006974

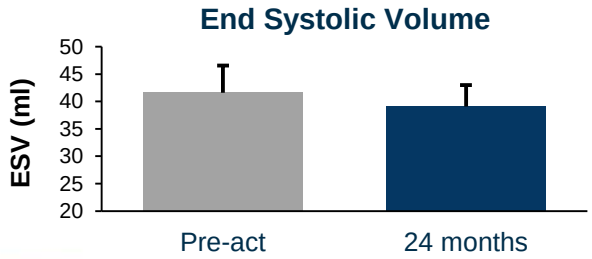
BackBeat® CNT – 2 Year Safety Results

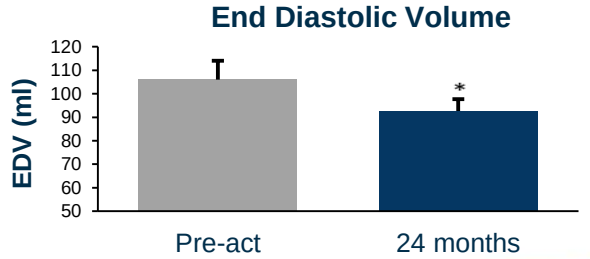
2 Year Safety Consistent with Expected Mechanism of Action

- Reduction in Heart Rate is indicative of reduced sympathetic activity
- Reduction in volumes with no change in EF suggests improvement of cardiac function









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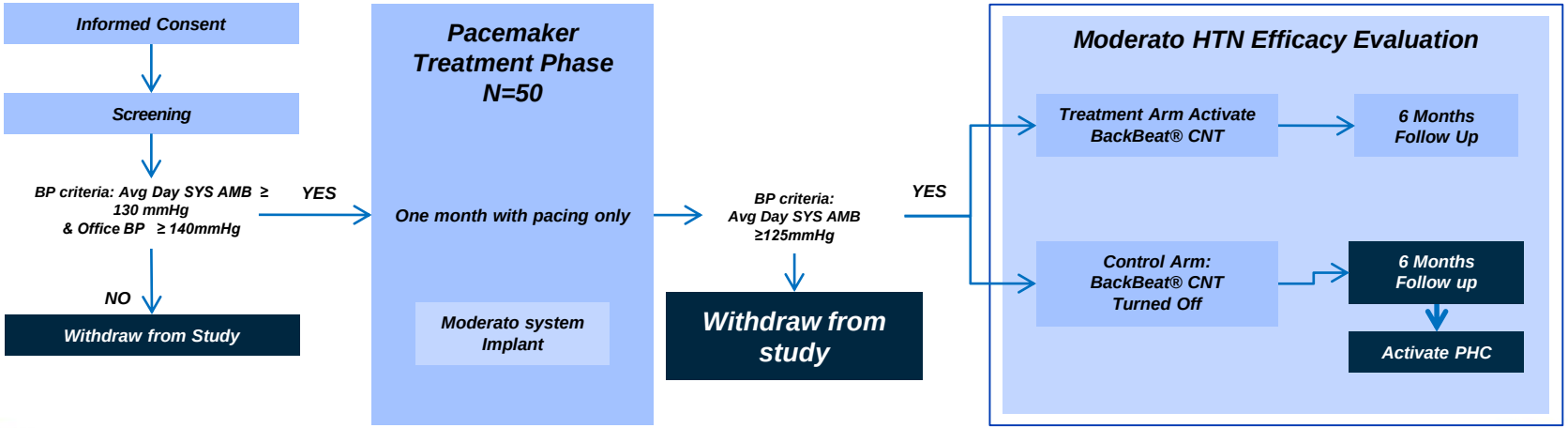
MODERATO II: Randomized, Controlled Study

- Prospective, 1:1 randomized double-blind active treatment (BackBeat® CNT) versus standard medical therapy
- Patient population: Uncontrolled blood pressure (office Systolic > 140, Day AMB BP > 130 mmHg) treated with at least one anti hypertension medication that are indicated for a dual chamber pacemaker
  - Primary Effectiveness Endpoint: Mean reduction in 24 hour systolic ambulatory blood pressure following 6 months of therapy
  - Primary Safety Endpoint: rate of MACE at 6 month between the treatment and control



BackBeat® CNT Program Update

BackBeat® CNT enables immediate, substantial and sustained lowering of blood pressure

- **2-year data from European MODERATO I study demonstrates significant and sustained efficacy of BackBeat® CNT**
- **Study met the safety endpoint. In addition, the safety data suggests improvement in cardiac function**
- **BackBeat CNT and Moderato IPG submitted for CE mark**
- **Randomized, double-blind MODERATO II study to further substantiate benefit of therapy:**
  - **Cohort I: European initial cohort (~50 patients) – results expected Q2 2019**
  - **Cohort II: Global, multicenter cohort (170 patients) – enrollment starts in Q4 2018**

THANK YOU!