# Orchestra BioMed Announces Initiation of BACKBEAT Pivotal Study of AVIM Therapy in Hypertensive Pacemaker Patients

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- *Orchestra BioMed and Medtronic, Inc., have an exclusive strategic collaboration for development and commercialization of AVIM therapy for hypertensive pacemaker population, which is estimated to be more than 750,000 patients annually worldwide*

NEW HOPE, Pa., Jan. 08, 2024 (GLOBE NEWSWIRE) -- Orchestra BioMed Holdings, Inc. (Nasdaq: OBIO, "Orchestra BioMed" or the "Company"), a biomedical company accelerating high-impact technologies to patients through risk-reward sharing partnerships, today announced the first patient was randomized in the BACKBEAT pivotal study in late December 2023. The BACKBEAT pivotal study will evaluate the efficacy and safety of atrioventricular interval modulation ("AVIM") therapy (also known as BackBeat CNT™), for the treatment of pacemaker-indicated patients with uncontrolled hypertension despite the use of antihypertensive medications.

AVIM therapy is an investigational patented bioelectronic therapy, administered using a standard dual-chamber pacemaker, designed to immediately, substantially and persistently reduce blood pressure. Orchestra BioMed and Medtronic, Inc. (NYSE: MDT) ("Medtronic") formed a strategic collaboration for the development and commercialization of AVIM therapy for hypertensive pacemaker patients in July 2022. If approved, Medtronic will have exclusive global rights to commercialize AVIM-enabled pacing systems for this target population, and Orchestra BioMed will share in the revenues generated from Medtronic sales of the AVIM-enabled pacing systems.

"Our collaboration with Orchestra BioMed will explore how cardiac pacing can go beyond management of bradycardia and conduction disease to treat hypertension as well," said Robert C. Kowal, M.D., Ph.D., vice president and general manager of Cardiac Pacing Therapies within the Medtronic Cardiac Rhythm Management operating unit. "Our goal is to deliver the best possible outcomes for patients; this study will help us understand the potential role of AVIM therapy in treating hypertension, a major source of cardiovascular illness and a comorbidity in more than 70% of patients receiving pacing therapy."

Suman Pasupuleti, M.D., from Citrus Cardiology Consultants, the first site to randomize a patient in the BACKBEAT pivotal study, commented: "Blood pressure management with currently available treatments is especially challenging in many elderly patients who also are prone to side effects from medications. This leaves a gap in the care of these patients and increases their risk for heart attack, stroke and heart failure progression. We are excited to be among the first to enroll patients in the BACKBEAT study, which will evaluate the efficacy and safety of this therapy in patients with high blood pressure who also need pacemakers."

"We are thrilled to announce the initiation of the BACKBEAT pivotal study. This is an essential milestone as we evaluate how this therapy may benefit pacemaker patients who confront the mortality and morbidity risks of elevated blood pressure," commented David Hochman, chairman, chief executive officer and founder of Orchestra BioMed. "We have activated multiple clinical sites and are screening patients in the U.S. and Europe. We are grateful to the clinical sites, our team and Medtronic for their dedication to finalizing all the study initiation deliverables. Most importantly, we are thankful to the patients who will participate in this landmark study."

The BACKBEAT pivotal study is a global, multi-center, prospective, randomized, double-blind study investigating the efficacy and safety of AVIM therapy in patients who have recently undergone implantation of a Medtronic dual-chamber cardiac pacemaker and have uncontrolled hypertension despite the use of antihypertensive medications. Orchestra BioMed is actively screening patients for enrollment in the BACKBEAT pivotal study. Site activations are expected to continue throughout 2024 with a target of activating approximately 80 centers in the U.S. and Europe. The study will randomize approximately 500 patients 1:1 to AVIM therapy combined with continued medical therapy (treatment) or continued medical therapy and standard pacing alone (control). The study's primary efficacy endpoint will determine at three months post-randomization whether AVIM-treated patients experience a statistically significant reduction in daily average blood pressure (mean 24-hour ambulatory systolic blood pressure or "aSBP") as compared to control patients. The primary safety endpoint will determine at three months post-randomization whether AVIM-treated patients experience serious adverse device effects that are not anticipated with cardiac pacing. Double-blind follow up will continue through 12 months to enable the collection of additional clinical endpoints. All patients will be eligible to cross over upon completion of the 12-month blinded follow-up phase.

The BACKBEAT pivotal study investigational device exemption ("IDE") was supported by encouraging results from MODERATO II, a prospective, multi-center, randomized, double-blind, pilot study of pacemaker patients with persistent hypertension conducted in Europe. MODERATO II showed that patients treated with AVIM therapy experienced net reductions of 8.1 mmHg in 24-hour aSBP

and 12.3 mmHg in office systolic blood pressure (oSBP) at six months when compared to control patients. There were no major adverse cardiac events in the treatment group, compared to three events in three patients in the control group (0.0% vs. 14.3%).[1]

More information on the BACKBEAT pivotal study can be found at: https://clinicaltrials.gov/study/NCT06059638.

**About Hypertension and the Risk of High Blood Pressure in the Pacemaker Population**

Hypertension ("HTN") is characterized by elevated blood pressure which increases the force of blood pushing against blood vessels, requiring the heart to work harder and consume more oxygen. HTN accelerates the progression of atherosclerosis and leads to increased risk of major cardiac events like heart attack, heart failure, kidney disease and other end organ damage. HTN is the leading global risk factor for death, affecting an estimated 1.28 billion adults worldwide. In the United States, 122 million adults, or approximately 47% of all adults, are estimated to have HTN. While many patients do not notice high blood pressure, cardiovascular risk doubles for every 10 mmHg increase in systolic blood pressure and the mortality rate doubles with an increase of 20 mmHg in systolic blood pressure.[2]

It is estimated that more than 70% of the approximately 1.1 million people globally who are implanted with cardiac pacemakers each year are also diagnosed with HTN. Based on updated American College of Cardiology/American Heart Association guidelines, an even higher percentage (approximately 80%) of U.S. patients that are indicated for the implant of a pacemaker have HTN. Pacemaker patients tend to be elderly and are more likely to suffer from co-morbidities such as atherosclerosis, hyperlipidemia, diabetes mellitus and chronic kidney disease, and harder to treat effectively with medical therapy for many reasons including co-morbidities and a high prevalence of isolated systolic HTN.

**About AVIM Therapy (BackBeat CNT™)**

AVIM therapy, also known as BackBeat CNT ™, is an investigational therapy compatible with standard dual-chamber pacemakers designed to substantially and persistently lower blood pressure. It has been evaluated in pilot studies in patients with hypertension who are also indicated for a pacemaker. MODERATO II, a double-blind, randomized, pilot study, showed that patients treated with AVIM therapy experienced net reductions of 8.1 mmHg in 24-hour ambulatory systolic blood pressure (aSBP) and 12.3 mmHg in office systolic blood pressure (oSBP) at six months when compared to control patients. The global IDE pivotal BACKBEAT (**B**radyc**A**rdia pa**C**ema**K**er with atrioventricular interval modulation for **B**lood pr**E**ssure tre**A**tmen**T**) study will further evaluate the safety and efficacy of AVIM therapy in lowering blood pressure in a similar target population of patients who have been indicated for, and recently implanted with, a dual-chamber cardiac pacemaker.

**About Orchestra BioMed**

Orchestra BioMed (Nasdaq: OBIO) is a biomedical innovation company accelerating high-impact technologies to patients through risk-reward sharing partnerships with leading medical device companies. Orchestra BioMed's partnership-enabled business model focuses on forging strategic collaborations with leading medical device companies to drive successful global commercialization of products it develops. Orchestra BioMed's lead product candidate is atrioventricular interval modulation (AVIM) therapy (also known as BackBeat Cardiac Neuromodulation Therapy (CNT™)) for the treatment of hypertension, a significant risk factor for death worldwide. Orchestra BioMed is also developing Virtue® Sirolimus AngioInfusion™ Balloon (SAB) for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. Orchestra BioMed has a strategic collaboration with Medtronic, one of the largest medical device companies in the world, for development and commercialization of AVIM therapy for the treatment of hypertension in pacemaker-indicated patients, and a strategic partnership with Terumo, a global leader in medical technology, for development and commercialization of Virtue SAB for the treatment of artery disease. Orchestra BioMed has additional product candidates and plans to potentially expand its product pipeline through acquisitions, strategic collaborations, licensing and organic development. For further information about Orchestra BioMed, please visit www.orchestrabiomed.com, and follow us on LinkedIn and X (formerly Twitter).

References to information included on, or accessible through, websites and social media platforms do not constitute incorporation by reference of the information contained at or available through such websites or social media platforms, and you should not consider such information to be part of this press release.

**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 enrollment, timing, implementation and design of the BACKBEAT pivotal study, the potential efficacy and safety of the Company's commercial product candidates, the ability of the Company's partnerships to accelerate clinical development, 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; failure to realize the anticipated benefits of the business combination; 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.*

**References:**


1. The formal final Data Safety Monitoring Board report for MODERATO II included a revised major adverse cardiac event rate in the control group from 9.5% to 14.3% to reflect another event of heart failure in a third control patient after publication of the study results. This report was provided to the FDA.
2. Benjamin EJ, Blaha MJ, Chiuve SE, et al., Heart Disease and Stroke Statistics – 2017 Update: A Report from the American Heart Association. Circulation. 2017; 135: e146.



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