Orchestra BioMed Granted FDA Approval of IDE to Initiate BACKBEAT Pivotal Study of BackBeat CNT™ for the Treatment of Hypertension in Pacemaker Patients

September 19, 2023

- *Hypertension is the most common comorbidity in the pacemaker population, affecting over 70% of patients or approximately 750,000 people annually worldwide*
- *Medtronic plc and Orchestra BioMed have an exclusive strategic collaboration for global development and commercialization of BackBeat Cardiac Neuromodulation Therapy™ (CNT), now also known as Atrioventricular Interval Modulation ("AVIM") therapy, for hypertensive pacemaker patients*
- *BACKBEAT global pivotal study is expected to start before the end of 2023*
- *IDE supported by data from the MODERATO II randomized pilot study that showed AVIM therapy drove significant and sustained reductions in blood pressure in hypertensive pacemaker patients*
- *Orchestra BioMed management to host conference call today, September 19, 2023, at 8:30am ET*

NEW HOPE, Pa., Sept. 19, 2023 (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 U.S. Food and Drug Administration ("FDA") granted approval of an investigational device exemption ("IDE") to initiate the global 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 evaluating the efficacy and safety of atrioventricular interval modulation ("AVIM") therapy (also known as BackBeat CNT™) for treating hypertensive patients who are indicated for a dual-chamber cardiac pacemaker.

Orchestra BioMed and Medtronic plc (NYSE: MDT) formed a strategic collaboration for the development and commercialization of AVIM therapy for hypertensive pacemaker patients in July 2022. Under the collaboration, Medtronic is providing Orchestra BioMed with development, clinical, and regulatory support for the BACKBEAT global pivotal study, which Orchestra BioMed is sponsoring. If approved, Medtronic will have exclusive global rights to commercialize AVIM-enabled pacing systems for this target population. Orchestra BioMed will share in the revenues generated from Medtronic sales of the AVIM-enabled pacing systems.

"We are thrilled to receive IDE approval from the FDA and move forward with plans to initiate the BACKBEAT global pivotal study, which is designed to support potential future regulatory review and potential approval of AVIM therapy for hypertensive patients indicated for a pacemaker. Achieving this milestone a little over a year after starting our strategic collaboration with Medtronic is a significant accomplishment for our company," said David Hochman, Chairman, Chief Executive Officer and Founder of Orchestra BioMed. "We believe this innovative therapy has the potential to substantially improve the standard of care for hypertensive pacemaker patients and we look forward to initiating the study before the end of 2023."

David Kandzari, M.D., Chief of the Piedmont Heart Institute and Chief Scientific Officer for Piedmont Healthcare, Atlanta, GA and Co-Principal Investigator for the BACKBEAT Study, commented: "Hypertension is the world's leading modifiable risk for death and affects over one billion people worldwide. While existing pharmaceutical treatments can be effective, more than half of individuals with hypertension do not meet blood pressure treatment goals. A device-based treatment like AVIM therapy has the potential to complement existing standards of care and reduce blood pressure to improve clinical outcome."

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 recently underwent a Medtronic dual-chamber cardiac pacemaker implant and have uncontrolled hypertension ("HTN") despite the use of antihypertensive medications. The study will randomize approximately 500 patients 1:1 to AVIM along with continued medical therapy and pacing (treatment) or continued medical therapy and pacing alone (control). The study's primary efficacy endpoint is the between group difference in the change of mean 24-hour ambulatory systolic blood pressure ("aSBP") at three months post randomization. The primary safety endpoint is freedom from unanticipated serious adverse device effects in the treatment arm at three months post-randomization. Double-blind follow up will continue through 12 months to enable collection of additional clinical endpoints. The Company plans to begin enrollment in the BACKBEAT study before the end of 2023, upon completion of standard clinical trial initiation activities, including clinical center Institutional Review Board approvals.

"Hypertension is the most common comorbidity in the pacemaker population, affecting more than 70% of patients. Patients who have pacemakers are generally older and at higher risk for major cardiovascular events. AVIM therapy represents a potentially transformative hypertension treatment for these patients since it can be administered using the same pacemaker they already need and managed by the same physicians already caring for them," commented Andrea Russo, M.D., Academic Chief, Division of Cardiology, Director of Cardiac Electrophysiology and Arrhythmia Services, Cooper University Hospital, and Co-Principal Investigator of the BACKBEAT Study, "We are excited to participate in the BACKBEAT study, which has been thoughtfully designed to evaluate the safety and efficacy of this novel therapy."

The BACKBEAT study IDE was supported by encouraging results from MODERATO II, a prospective, multi-center, randomized, double-blind, pilot study of pacemaker patients with persistent HTN. 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.

Video Webcast Information

Orchestra BioMed will host a video webcast with slides today, September 19, 2023, at 8:30 a.m. ET to discuss the BACKBEAT Pivotal Study. This webcast can be accessed by clicking on the Events page of the Company's website, and this press release will be archived on the News Releases page. Within two hours of the webcast, a replay of the webcast and accompanying slides will be available on the Events page.

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.

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 ACC/AHA 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 planned global 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 flagship product candidates include Atrioventricular Interval Modulation (AVIM) therapy (BackBeat CNT) for the treatment of hypertension, the leading risk factor for death worldwide, and Virtue® Sirolimus AngioInfusion™ Balloon (SAB) for the treatment of atherosclerotic coronary 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 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 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; 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.

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