Orchestra BioMed Announces Presentation of Results from Clinical Study Demonstrating Favorable Hemodynamic Effects of AVIM Therapy In Hypertensive Pacemaker Patients

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- *Clinical study evaluated impact of AVIM therapy as compared to standard pacing using invasive pressure-volume loop analysis in 16 hypertensive pacemaker-indicated patients*
- *Results demonstrate statistically significant reductions in systolic blood pressure, intra-cardiac volumes, total peripheral resistance and stroke work, with no significant changes in stroke volume or contractility.*
- *AVIM therapy showed consistent favorable hemodynamic effects using both conduction system pacing, as well as traditional right ventricular lead placements*
- *Orchestra BioMed is actively enrolling patients in the BACKBEAT pivotal study of AVIM therapy in hypertensive pacemaker patients in collaboration with Medtronic*

NEW HOPE, Pa., March 06, 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 presentation of new clinical data from a pressure-volume ("PV") loop study of atrioventricular interval modulation ("AVIM") therapy (also known as BackBeat CNT™) in pacemaker-indicated patients with uncontrolled hypertension despite the use of antihypertensive medication. These data demonstrate the favorable impact of AVIM therapy compared to standard right ventricular (RV) pacing on systolic blood pressure and overall cardiac function when delivered using both conduction system andstandard pacing lead locations. The PV loop study was conducted at Na Homolce Hospital in Prague by Prof. Petr Neužil, M.D. and the data were featured in an oral presentation at the Technology and Heart Failure Therapeutics ("THT") 2024 Meeting by Prof. Karl-Heinz Kuck, M.D., Medical Director at LANS Cardio Hamburg.

AVIM therapy is an investigational patented bioelectronic therapy, administered using a standard dual-chamber pacemaker, designed to immediately, substantially and persistently reduce blood pressure.

"These results showcase the innovative mechanism of action of AVIM therapy, which acts through well-characterized physiologic mechanisms to substantially reduce blood pressure and favorably impact circulatory hemodynamics," commented Professor Kuck. "Well-conducted invasive PV loop studies are a robust way to evaluate the impact of a novel therapy like AVIM on hemodymanics and overall cardiac function. Results from this study in hypertensive pacemaker patients showing significant decreases in systolic blood pressure, intra-cardiac volumes, total peripheral resistance and cardiac workload, without compromising cardiac output or contractility are encouraging and consistent with the therapy's intended effect. It is also important that these favorable effects occur using both traditional pacing lead locations, as well as conduction system lead positions, which are rapidly emerging as the preferred approach for ventricular pacing given potential benefits to patient safety. These results, in addition to the promising results from prior long-term clinical studies, heighten our excitement about the BACKBEAT global pivotal study that is now underway."

Summary of the PV Loop Clinical Results Presented at THT 2024

Design

- 16 patients indicated for a dual-chamber pacemaker who also had uncontrolled hypertension despite the use of antihypertensive medication underwent invasive PV loop testing to evaluate cardiac function, measured by changes in left ventricular ("LV") volumes and pressures using a pressure-volume catheter placed in the LV.
- Systolic blood pressure ("SBP") was measured using a pressure transducer placed in the aorta, and baseline measurements were recorded using atrial pacing at a fixed rate and normal conduction
- AVIM therapy with pacing leads placed in standard RV locations ("AVIM RV"), as well as in conduction system pacing ("AVIM CSP") locations targeting the left bundle branch area (LBBA) regions, respectively, was compared to standard AV sequential pacing (DDD mode pacing or "AV Pacing").

Results

Overall mean results for each variable were calculated using paired measurements for each individual patient using AVIM RV, AVIM CSP and AV Pacing, respectively:

- **AVIM therapy generated statistically significant reductions (*p<0.05*) in SBP, end diastolic volume ("EDV"), end diastolic pressure ("EDP"), and end systolic volume ("ESV") using both AVIM RV and AVIM CSP pacing lead locations compared to AV Pacing**
  - SBP was reduced by 17.1 mmHg and 19.2 mmHg compared to 1.6 mmHg
  - EDV was reduced by 12.6 mL and 18.6 mL compared to 1.4 mL
  - EDP was reduced by 2.3 mmHg and 3.6 mmHg compared to an increase of 0.3 mmHg
  - ESV was reduced by 11.0 mL and 14.1 mL compared to an increase of 1.8 mL

- **AVIM therapy drove statistically significant (*p<0.05*) reductions in stroke work (SW) without significantly reducing stroke volume (SV) compared to AV Pacing**
    - Stroke work (SW) was reduced by 1596 mL and 1870 mL compared to 42 mL
    - Stroke volume (SV) was not significantly reduced by AVIM RV, AVIM CSP or AV Pacing
- **AVIM therapy drove statistically significant (*p<0.05*) reductions in total peripheral resistance ("TPR", measured by Ea) and no change in contractility ("Ees") compared to AV Pacing**
    - Effective arterial elastance ("Ea", a measure of TPR) was reduced by 0.23 mmHg/mL and 0.31 mmHg/mL compared to an increase of 0.04 mmHg/mL
    - Ees remained unchanged with AVIM RV, AVIM CSP and AV Pacing

Orchestra BioMed and Medtronic plc (NYSE: MDT) ("Medtronic") formed a strategic collaboration for the development and commercialization of AVIM therapy for hypertensive pacemaker patients in July 2022. If AVIM therapy is approved by the U.S. Food and Drug Administration, 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.

Orchestra BioMed is actively enrolling patients in the BACKBEAT pivotal study, 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. The study's primary efficacy endpoint will determine at three months post-randomization whether AVIM-treated patients experience a statistically significant reduction in aSBP as compared to control patients. 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.[1]

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.

References to Websites and Social Media Platforms

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; risks related to regulatory approval of the Company's product candidates and ongoing regulation of the Company's product candidates, if approved; 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. 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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