Orchestra BioMed™ Announces Presentations at TCT 2021 of Positive Long-Term Clinical Results from the MODERATO II Study Showing the Significant Clinical Impact of BackBeat CNT™ on Isolated Systolic Hypertension and Pulse Pressure

November 5, 2021

BackBeat CNT treated patients experienced a mean reduction of 17.5 mmHg in office systolic blood pressure measured 24-months following therapy activation.

Patients with Isolated Systolic Hypertension (ISH) treated with BackBeat CNT experienced clinically meaningful and statistically significant reductions of 7.4 mmHg in ambulatory systolic blood pressure and 9.4 mmHg in ambulatory Pulse Pressure at 6 months compared to controls.

ISH is the predominant form of hypertension in patients over 60 years old and the most challenging to treat; elevated Pulse Pressure is a significant, independent risk factor of coronary heart disease.

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New Hope, PA, November 5, 2021 – Orchestra BioMed™, Inc., ("Orchestra BioMed" or the "Company"), a biomedical innovation company focused on developing transformative therapeutic products for large unmet clinical needs in procedure-based medicine, today announced multiple presentations of long-term clinical results and ISH subgroup data from the MODERATO II study of BackBeat Cardiac Neuromodulation Therapy™ (BackBeat CNT™) in patients with hypertension and an indication for a pacemaker at the Transcatheter Cardiovascular Therapeutics (TCT) 2021 annual conference being held in-person in Orlando, Florida, and virtually from November 4 – 6, 2021.

Results showed a mean reduction of 17.5 mmHg in office systolic blood pressure (oSBP) among all BackBeat CNT treated patients who completed 24-month follow-up. The previously reported primary endpoint of the 6-month double-blind, randomized portion of the trial demonstrated that BackBeat CNT treated patients experienced a clinically meaningful and statistically significant reduction of 12.3 mmHg in oSBP and 8.1 mmHg in 24-hour ambulatory systolic blood pressure (aSBP) when compared to control patients (p=0.02, p=0.01). In a subgroup of patients with ISH, a dangerous and challenging to treat form of hypertension prevalent in older patients, treatment with BackBeat CNT resulted in clinically meaningful and statistically significant reductions of 7.4 mmHg in aSBP and 11.9 mmHg in oSBP when compared to control (continued medical therapy) patients at 6 months. Further, in patients with ISH, BackBeat CNT drove statistically significant reductions of 9.4 mmHg in ambulatory Pulse Pressure and 13.3 mmHg in office Pulse Pressure at 6 months as compared to control patients.

"We are very encouraged by the exploratory findings highlighting BackBeat CNT's impact in patients with ISH, particularly since a substantial reduction in Pulse Pressure can dramatically lower overall cardiovascular risk," said Daniel Burkhoff, M.D., Ph.D., Director of Heart Failure, Hemodynamics and Mechanical Circulatory Support Research at Cardiovascular Research Foundation, who presented the study findings. "The results from the MODERATO II study offer compelling preliminary evidence that BackBeat CNT may provide a safe and effective therapy for ISH, which is the most common form of hypertension in older patients and one that is difficult to treat. The challenging nature of ISH often leads to the exclusion of these patients from hypertension therapy studies and contributes to their position as the majority of inadequately treated hypertension patients."

MODERATO II was a European prospective, multi-center, double-blind study investigating the efficacy of BackBeat CNT™ in patients with persistent hypertension (aSBP ≥130 mmHg and office systolic blood pressure (oSBP) ≥140 mmHg) despite one or more anti-hypertensive medications. Following a 30-day run-in period, during which patients received only standard pacing along with anti-hypertensive medications, 47 patients who met follow-up screening criteria for daytime aSBP were randomized to BackBeat CNT (n=26) or control (n=21) groups. Due to the advanced age and general poor health of the pacemaker population, the majority of the patients enrolled in the study had ISH, 23 patients in the treatment arm (88.5%) and 15 patients in the control arm (71.4%). ISH is defined as an oSBP >140 mmHg and diastolic BP <90 mmHg. Although patients with ISH were not a prespecified subgroup, exploratory findings revealed statistically significant improvements in aSBP, oSBP and Pulse Pressure in ISH patients treated with BackBeat CNT as compared to control. Additional key findings from study participants with ISH include:

- Mean aSBP was reduced by 9.5 mmHg in the BackBeat CNT group as compared to a reduction of 2.1 mmHg in the control group, a net treatment effect of 7.4 mmHg (p=0.03) at 6 months.
- Mean oSBP was reduced by 10.6 mmHg in the BackBeat CNT group as compared to an increase of 1.4 mmHg in the control group, a net treatment effect of 11.9 mmHg (p=0.04) at 6 months.
- A significant reduction in oSBP of 15.8 mmHg was sustained out to 24 months in the treatment group in open label follow-up after the end of the 6 months randomized portion of the study.
- There was a significant reduction in ambulatory Pulse Pressure of 9.4 mmHg in BackBeat CNT treated patients at 6 months vs. control (p=0.01).
- There was significant reduction in office Pulse Pressure of 13.3 mmHg in BackBeat CNT treated patients at 6 months vs. control (p<0.01); a reduction of 13.9 mmHg was sustained at 24 months in the treatment group in open label follow-up.
- Overall, there was a very low rate of major adverse cardiac events (MACE), with no events in the treatment group and two events in the control group (no statistical difference between groups at 6 months).

“We are excited by BackBeat CNT’s significant and durable impact on blood pressure in the MODERATO II study,” said David Hochman, chairman and CEO of Orchestra BioMed. “The effects on ISH and Pulse Pressure are especially compelling given the prevalence of this particularly challenging form of hypertension in our initial target population of hypertensive patients indicated for a permanent pacemaker implant. We look forward to communicating next steps as we work to advance BackBeat CNT into definitive studies and towards regulatory approval.”

About Isolated Systolic Hypertension, Elevated Pulse Pressure and Pacemaker Patients

Based on data from the National Health and Nutrition Examination Survey (NHANES) III, 74.5% of U.S. adults over 60 years old have hypertension, with over 65% of them suffering from ISH. ISH patients have elevated systolic blood pressure (>140 mmHg), while their diastolic blood pressure remains normal or low (≤90 mmHg). ISH is a more difficult to treat form of hypertension because antihypertensive medications generally impact both systolic and diastolic pressure. It is estimated that over 80% of treatment failure patients over 60 years old have ISH.1 ISH patients experience elevated Pulse Pressure (the difference between systolic and diastolic pressures), which is a known significant, independent risk factor for coronary heart disease. According to published literature, a 10 mmHg increase in Pulse Pressure is associated with a 32% increase in risk of heart failure and a 24% increase in risk of stroke (after controlling for systolic BP and other risk factors)2. In addition, in men ≥60 years old (which happens to be the typical age of pacemaker patients), risk for coronary artery disease is three times larger in patients with Pulse Pressure of ≥70 mmHg compared to those with Pulse Pressure of 60 mmHg3.

Over 1.1 million pacemakers are implanted annually worldwide.4 More than 70% of patients indicated for a pacemaker suffer from hypertension.5 Given that pacemaker-indicated patients are typically older, it is estimated that the majority of hypertensive pacemaker patients suffer from ISH.1

About BackBeat CNT™

BackBeat CNT, a flagship therapy of Orchestra BioMed, is a bioelectronic treatment designed to immediately, substantially, and persistently lower blood pressure (BP) while simultaneously modulating the Autonomic Nervous System (ANS). Orchestra BioMed’s CE Mark-approved Moderato® implantable pulse generator system delivers BackBeat CNT while also providing standard pacemaker functions. BackBeat CNT is designed to mimic the effects of multi-drug hypertension therapy by targeting preload, afterload and sympathetic tone. The initial target treatment population for BackBeat CNT is patients with uncontrolled hypertension who are also indicated for a pacemaker. BackBeat CNT has the potential to be integrated into any dual-chamber pacemaker system, making this therapy highly suitable for Orchestra BioMed’s risk-reward sharing strategy of pursuing commercialization through a strategic partnership with a leading cardiac rhythm management company.

About Orchestra BioMed™

Orchestra BioMed is a biomedical innovation company focused on developing transformative therapeutic products for large unmet needs in procedure-based medicine. The Company is led by a highly accomplished, multidisciplinary management team and board of directors with extensive experience in all phases of medical device development. 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 was formed in 2018 by assembling a pipeline of multiple late-stage clinical product candidates originally developed by the Company’s founding team. The Company’s flagship product candidates are Virtue® Sirolimus AngioInfusion™ Balloon (SAB) for the treatment of artery disease, the leading cause of mortality, and BackBeat Cardiac Neuromodulation Therapy™ for the treatment of hypertension, the leading risk factor for death worldwide. Orchestra BioMed has a global strategic partnership with Terumo Corporation, one of the world’s largest medical device companies, for development and commercialization of Virtue SAB. The Company has additional product candidates in its pipeline and plans to thoughtfully expand its product pipeline in the future through acquisitions, strategic collaborations, licensing, and organic development.

Forward-Looking Statements

Some of the statements made herein constitute forward-looking statements. These statements relate to future financial and other performance or anticipated plans and are identified by words such as “may,” “will,” “should,” “expect,” “could,” “scheduled,” “plan,” “intend,” “anticipate,” “believe,” “estimate,” “potential,” “propose” and “continue” or negative variants of such terms. These and similar forward-looking statements discuss the Company’s future expectations and plans. 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. These statements are only estimates of future performance. Actual performance or events may not meet such expectations or estimates and may, in fact, differ materially.

Although the Company believes that the expectations reflected in the forward-looking statements made herein are reasonable, the Company cannot and does not guarantee future results, levels of activity, performance, or achievements. Moreover, the Company does not assume any responsibility for the accuracy and completeness of such forward-looking statements in the future. The Company does not plan and, subject to applicable law, undertakes no obligation to update any of the forward-looking statements made herein.

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