Orchestra BioMed Announces Publication of Clinical Data Demonstrating Favorable Blood Pressure and Hemodynamic Effects of AVIM Therapy in JACC: Clinical Electrophysiology

August 26, 2025

- *Data from acute and chronic pressure-volume loop studies support the mechanism of action and show a favorable impact of AVIM therapy on blood pressure and cardiovascular hemodynamics*
- *AVIM therapy drove statistically significant reductions in systolic blood pressure, intra-cardiac volumes, total peripheral resistance and stroke work, with no adverse impact on stroke volume or contractility.*
- *Orchestra BioMed and Medtronic (NYSE: MDT) have a strategic collaboration for the development of AVIM therapy for treatment of uncontrolled hypertension in patients indicated for a pacemaker; over 750,000 patients annually that receive pacemakers worldwide are also believed to have hypertension.*
- *AVIM therapy has FDA Breakthrough Device Designation for the treatment of uncontrolled hypertension in patients with increased cardiovascular risk, a population the Company estimates to comprise over 7.7 million patients in the U.S.*

NEW HOPE, Pa., Aug. 26, 2025 (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 publication of data in the *Journal of the American College of Cardiology: Clinical Electrophysiology* ("JACC: Clinical EP") from a pressure-volume ("PV") loop study demonstrating favorable hemodynamic effects of AVIM therapy in pacemaker-indicated patients with uncontrolled hypertension. AVIM therapy is currently being evaluated in the BACKBEAT global pivotal study, which Orchestra BioMed is conducting in collaboration with Medtronic, to support potential future global regulatory approvals and commercialization of AVIM therapy-enabled devices.

The publication, titled "*Pressure-Volume Analysis Demonstrates Short- and Long-Term Hemodynamic Effects of Atrioventricular Interval Modulation Therapy in Hypertension,*" reports findings from an invasive PV loop analysis in 16 hypertensive pacemaker-indicated subjects, as well as noninvasive PV loop analysis from a subgroup of subjects (n=32) from the MODERATO II study receiving chronically administered AVIM therapy. The analyses demonstrated that AVIM therapy reduced systolic blood pressure ("SBP") acutely by decreasing cardiac preload and effective arterial elastance unrelated to pacing lead location, while also improving left ventricular ("LV") end-diastolic and end-systolic volumes. Chronically administered AVIM therapy demonstrated sustained reductions in SBP and end-diastolic volume, indicative of favorable reverse LV remodeling. Results also demonstrated consistently favorable hemodynamic effects using traditional right ventricular ("RV") and conduction system pacing ("CSP") lead placements.

Daniel Burkhoff, M.D., Ph.D., Director, Heart Failure, Hemodynamics, and MCS Research, Cardiovascular Research Foundation and a manuscript author commented: "Pressure-volume loop analysis is regarded as the gold standard for assessing systolic and diastolic function as well as reverse remodeling. These results provide powerful insights on the impact of AVIM therapy to both decrease blood pressure and favorably impact ventricular end-diastolic volume without compromising cardiac output or increasing workload. Notably, these favorable effects were observed consistently and with different pacing lead locations, demonstrating the versatility of AVIM therapy. Publication of these data in a prestigious peer-reviewed journal such as *JACC: Clinical Electrophysiology* provides further validation from the clinical community reinforcing the therapeutic rationale behind AVIM therapy and further highlighting its potential to deliver differentiated clinical benefit for patients with uncontrolled hypertension."

Key findings include:

- **Significantly reduced (p<0.05) systolic blood pressure ("SBP")**: average decreases of **17.1 mmHg** (AVIM via RV pacing) and **19.2 mmHg** (AVIM via CSP), compared to **1.7 mmHg** with standard dual-chamber pacing.
- **Improved left ventricular hemodynamics with both RV pacing and CSP, respectively, compared to standard pacing**:
  - End-diastolic volume significantly decreased by 12.6 mL and 18.6 mL compared to 1.4 mL
  - End-systolic volume significantly decreased by 11.0 mL and 14.1 mL compared to an increase of 1.8 mL
  - End-diastolic pressure significantly decreased by 2.1mmHg and 3.9 mmHg, compared to an increase of 0.3 mmHg
- **Significantly reduced (p<0.05) cardiac workload**: Stroke work decreased by 1,596 mL (RV) and 1,870 mL (CSP), compared to 42mL (standard pacing), with minimal impact on stroke volume.
- **Significantly reduced total peripheral resistance ("TPR", measured by Ea):**
  - Effective arterial elastance ("Ea") decreased by 0.23 mmHg/mL (RV) and 0.31 mmHg/mL (CSP), compared to an increase of 0.04 mmHg/mL (standard pacing).

Yuval Mika, Ph.D., Executive Vice President, Bioelectronic Therapies at Orchestra BioMed, stated, "The publication of the PV loop data in *JACC: Clinical Electrophysiology* marks another important milestone showcasing AVIM therapy's potential ability to significantly reduce blood pressure and favorably impact cardiac function in hypertensive patients with increased cardiovascular risk. The consistent reduction seen in cardiac preload, as well as cardiac afterload with both CSP and RV lead placements in these pilot studies demonstrates that AVIM therapy's mechanism of action works regardless of lead location. Furthermore, acute and chronic PV loop results indicate AVIM therapy's potential to induce positive reverse remodeling of ventricular hypertrophy, highlighting potential to prevent or even treat heart failure. We continue to believe that AVIM therapy has the potential to reshape the standard of care for higher risk patients with uncontrolled hypertension in the pacemaker population and beyond."

The full article is available online in *JACC: Clinical Electrophysiology*.

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, the leading risk factor for death worldwide. Orchestra BioMed is also developing the 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. 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.

About AVIM Therapy

AVIM therapy 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. In addition to reducing blood pressure, clinical results using AVIM therapy demonstrate improvements in cardiac function and hemodynamics. The BACKBEAT (BradycArdia paCemaKer with atrioventricular interval modulation for Blood prEssure treAtmenT) global pivotal study will evaluate the safety and efficacy of AVIM therapy in lowering blood pressure in patients who have systolic blood pressure above target despite anti-hypertensive medication and who are indicated for or have recently received a dual-chamber cardiac pacemaker. AVIM therapy has been granted Breakthrough Device Designation by the FDA for the treatment of uncontrolled hypertension in patients who have increased cardiovascular risk.

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. 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 annual report on Form 10-K for the year ended December 31, 2024, which was filed with the Securities and Exchange Commission on March 31, 2025, 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.

Investor Contact
Silas Newcomb
Orchestra BioMed
Snewcomb@orchestrabiomed.com

Media Contact
Kelsey Kirk-Ellis
Orchestra BioMed
Kkirkellis@orchestrabiomed.com