Orchestra BioMed Demonstrates Strength of Cardiovascular Pipeline with Virtue® SAB and AVIM Therapy Presentations at CRT 2024 Annual Meeting

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- *New pharmacokinetic data demonstrate Virtue® SAB enables extended release of sirolimus above required tissue concentrations in target arterial sites without polymer degradation or detectable remaining polymer within 90 days of balloon delivery*
- *AVIM therapy presentation highlighted recent clinical results showing favorable hemodynamic effects and long-term reduction in 24-hour ambulatory systolic blood pressure, as well as the design of the BACKBEAT global pivotal study now enrolling in collaboration with Medtronic, plc (NYSE:MDT)*

NEW HOPE, Pa., March 13, 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 two oral presentations were given at the Cardiovascular Research Technologies ("CRT") 2024 Meeting in Washington, D.C. One presentation featured new preclinical pharmacokinetic ("PK") data on Virtue ® Sirolimus AngioInfusion Balloon ("SAB"), a novel drug-eluting balloon angioplasty system designed to deliver a proprietary, extended-release formulation of sirolimus, SirolimusEFR™ to the vessel wall during balloon angioplasty without any coating on the balloon surface. A second presentation featured recently reported clinical data on atrioventricular interval modulation ("AVIM") therapy (also known as BackBeat CNT), an investigational therapy delivered via standard dual-chamber pacemakers designed to immediately, substantially and persistently lower blood pressure. The AVIM presentation also outlined the design of the currently enrolling BACKBEAT global pivotal study evaluating AVIM therapy in hypertensive pacemaker patients in collaboration with Medtronic.

Virtue SAB Oral Presentation, *presented by Dean Kereiakes, M.D., President and Medical Director of The Christ Hospital Heart and Vascular Institute and Professor of Clinical Medicine at The Ohio State University*

Dr. Kereiakes' presentation, focused on the role of drug-coated and drug-eluting balloon angioplasty systems for the treatment of coronary in-stent restenosis ("ISR"), outlined key points of differentiation and potential advantages for Virtue SAB, including:

- No surface drug coating and, therefore, no drug loss in-transit to a target arterial lesion or creation of large particulates during balloon inflation
- Focal uptake and extended release of sirolimus at tissue concentrations greater than the 1 ng/mg tissue concentration known to be required for effective control of cellular proliferation through the critical healing period.
    - Supported by published preclinical data of over 750 coronary artery balloon treatments
- New preclinical PK data demonstrating that Sostenocel™, the proprietary polymer system enabling Virtue SAB's SirolimusEFR, was shown to be eliminated in SirolimusEFR-treated stented arteries without detectable degradation, which can lead to localized tissue inflammation. Specifically, the presented PK data showed that:
    - Sostenocel was undetectable at 90 days in treated arteries and at 3 days in all non-target tissues
    - Molecular weight of Sostenocel remained unchanged prior to elimination, showing no evidence of in-vivo degradation.

"Virtue SAB represents a therapeutic innovation that may provide a reliable method to deliver the proven benefits of sirolimus, the gold standard therapeutic used in drug-eluting stents, during balloon angioplasty for the treatment of coronary in-stent restenosis without the potential risks associated with a permanent metal implant or a balloon surface coating," commented Dr. Kereiakes. "Realizing the advantages of sirolimus requires a novel solution that enables sufficient drug uptake and extended drug release at necessary tissue concentrations through the 30-day critical healing period post-procedure. The preclinical data presented at CRT demonstrate how the Sostenocel polymer system that enables SirolimusEFR, the proprietary drug formulation used in Virtue SAB, is eliminated prior to degradation, enabling the long-term pharmacokinetics to support sirolimus arterial tissue concentrations that are essential for effective prevention of restenosis without the inflammatory risks associated with polymer degradation."

The U.S. Food and Drug Administration granted Orchestra BioMed a conditional Investigational Device Exemption ("IDE") to initiate the Virtue ISR-US pivotal study evaluating the efficacy and safety of Virtue SAB for the treatment of patients with coronary ISR. Orchestra BioMed and Terumo, the Company's strategic partner for the development and commercialization of Virtue SAB in coronary and peripheral artery disease, are currently working to update operational plans and financial arrangements for execution of this and other pivotal studies in the future.

AVIM Therapy Oral Presentation, *presented by Dan Burkhoff, M.D., Ph.D., Director, Heart Failure, Hemodynamics, and MCS Research, Cardiovascular Research Foundation*

Dr. Burkhoff presented an overview of the AVIM therapy program in hypertensive pacemaker patients, including:

- The BACKBEAT global pivotal study design

- Recently reported clinical results from a long-term follow-up study showing sustained reductions of 8.9 mmHg in 24-hour ambulatory systolic blood pressure at a mean of 3.6 years from treatment activation in AVIM-treated patients
- Results from a new clinical study evaluating the impact of AVIM therapy compared to standard pacing using invasive pressure-volume loop analysis in 16 hypertensive pacemaker-indicated patients. AVIM therapy demonstrated:
    - Consistent favorable hemodynamic effects using both conduction system, as well as traditional right ventricular lead placements.
    - 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.

"The new data showing the long-term durability of blood pressure reduction in AVIM-treated patients, as well as the clear, favorable hemodynamic impact of AVIM therapy's mechanism of action reinforces my belief in the potential benefit this novel therapy can offer hypertensive patients in the pacemaker population and beyond," said Dr. Burkhoff. "These data combined with previous clinical results from the MODERATO I and II studies are encouraging and bolster my confidence in the potential outcomes of the BACKBEAT global pivotal study, which is a well-designed prospective, double-blind, randomized study evaluating this innovative therapy and currently enrolling hypertensive pacemaker patients in the U.S. and EU."

Orchestra BioMed is actively enrolling patients in the BACKBEAT global pivotal study of AVIM therapy in pacemaker-indicated patients who also have hypertension despite the use of antihypertensive medications.

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.

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