Orchestra BioMed Announces First Patients Enrolled in Virtue® SAB US Pivotal IDE Coronary Trial

October 27, 2025

- *Orchestra BioMed's Virtue® Sirolimus AngioInfusion™ Balloon ("Virtue SAB") is the first non-coated drug-eluting balloon system designed to deliver a large liquid dose of proprietary extended-release sirolimus ("SirolimusEFR™")*
- *The Virtue Trial is the first U.S. investigational device exemption ("IDE") head-to-head randomized coronary pivotal trial evaluating a sirolimus-eluting balloon versus a commercially available paclitaxel-coated balloon (AGENT™)*
- *Coronary in-stent restenosis ("ISR"), the clinical focus of the Virtue Trial, is a difficult-to-treat and serious complication of coronary stenting that increases the risk of life-threatening heart problems, affecting an estimated 100,000 patients in the U.S. annually*
- *Virtue SAB has FDA Breakthrough Device Designation for the treatment of coronary ISR, as well as for coronary small vessel disease and below-the-knee peripheral artery disease*

NEW HOPE, Pa., Oct. 27, 2025 (GLOBE NEWSWIRE) -- Orchestra BioMed Holdings, Inc. (Nasdaq: OBIO, "Orchestra BioMed" or the "Company"), a biomedical company accelerating high-impact technologies to patients through strategic partnerships with market-leading global medical device companies, today announced the first patient enrollments in the *Virtue SAB in the Treatment of Coronary ISR Trial* ("Virtue Trial"), the Company's U.S. IDE pivotal trial comparing its highly differentiated Virtue® Sirolimus AngioInfusion™ Balloon ("Virtue SAB") to the AGENT paclitaxel-coated balloon, currently the only drug-coated balloon ("DCB") FDA-approved for a coronary indication. The initial cases were successfully completed by the teams at The Christ Hospital Heart & Vascular Institute in Cincinnati, OH, and St. Francis Hospital & Heart Center in Roslyn, NY, marking the initiation of the Virtue Trial. Dean J. Kereiakes, M.D., FACC, MSCAI, Chairman of The Christ Hospital Heart & Vascular Institute and Medical Director of The Christ Hospital Research Institute and Allen Jeremias M.D., Director of Interventional Cardiology Research and Associate Director, Cardiac Catheterization Laboratory, St. Francis Hospital & Heart Center are co-principial investigators of the Virtue Trial. Designed to support regulatory approval of Virtue SAB, the Virtue Trial is expected to enroll 740 patients at up to 75 centers in the United States with enrollment completion currently planned for mid-2027.

Virtue SAB: Redefining Delivery of Sirolimus

"Virtue SAB and SirolimusEFR were specifically designed to optimize the dose, delivery, uptake and extended release of sirolimus without the limitations of a drug coating on the balloon surface. A substantial body of clinical evidence from drug-eluting stent studies has established sirolimus and its analogs as the gold-standard drug for promoting vessel healing and preventing restenosis following interventional procedures," said Jarrod D. Frizzell, MD, MS, FACC, FSCAI, Director of Complex Coronary Therapeutics, Interventional Cardiology, The Christ Hospital Health Network. "The Virtue Trial will allow us to evaluate the performance of this fundamentally different approach to delivering sirolimus, which has shown promising results in a prior pilot clinical study in coronary ISR treatment, in direct comparison to the AGENT paclitaxel-coated balloon."

Additionally, Dr. Jeremias commented, "Drug coated balloons offer a promising alternative to drug-eluting stents for the treatment of coronary indications such as coronary ISR. Virtue SAB and SirolimusEFR are designed to go beyond DCBs with the goal of optimizing drug dosing, tissue uptake and extended drug bioavailability at the site of treatment. Our team at St. Francis is excited to play a leadership role in the Virtue Trial which will evaluate this differentiated, non-coated drug-delivery system head-to-head versus the current market leading DCB."

Virtue SAB is designed to deliver a large liquid dose of a proprietary extended-release formulation of sirolimus, SirolimusEFR™, through a non-coated microporous AngioInfusion™ Balloon that protects the drug in transit and helps overcome certain limitations of DCBs. SirolimusEFR™ is designed to enable enhanced tissue uptake and extended release of therapeutic levels of sirolimus through the critical healing period, exceeding previously published target tissue concentrations of proven drug-eluting stents. In the multi-center SABRE pilot study, Virtue SAB demonstrated promising clinical results for the treatment of single-layer coronary ISR:

- 12-month target lesion failure of 2.8%
- Zero target lesion revascularizations from 12-month follow-up through 36-month follow-up; and
- 6-month late lumen loss of 0.12mm.

Virtue SAB has FDA Breakthrough Device Designation for the treatment of coronary ISR, as well as for coronary small vessel disease and below-the-knee peripheral artery disease. Orchestra BioMed estimates the total global market opportunity for drug-eluting balloons to be over $10 billion annually.

A Head-to-Head Randomized Evaluation of a Sirolimus-Eluting Balloon vs. a Paclitaxel-Coated Balloon
The Virtue Trial is a prospective, multi-center, randomized trial comparing clinical outcomes of Virtue SAB to AGENT Paclitaxel DCB in the treatment of coronary ISR. Data from the Virtue Trial is expected to be used to support regulatory approval in the U.S. The primary endpoint is a non-inferiority comparison of Target Lesion Failure (TLF) defined as a composite of cardiac death, nonfatal target vessel myocardial infarction and ischemia-driven target lesion revascularization at 12 months. The trial is expected to randomize 740 patients across up to 75 centers in the U.S.

Darren R. Sherman, President and Chief Operating Officer of Orchestra BioMed stated, "We believe the future of arterial disease treatment will be driven by optimized delivery and extended tissue release of therapeutic doses of sirolimus, the proven antiproliferative drug with well-established safety and effectiveness. Balloon surface-coating drug delivery has challenges and limitations, including dosing constraints, drug-loss that requires rapid device navigation, and the release of large embolic particulates. We designed Virtue SAB and its key enabling technology, our proprietary SirolimusEFR, to overcome these limitations and realize the full potential of arterial drug delivery during angioplasty. With the launch of the Virtue Trial, we're taking a major step toward realizing our vision of improving patient outcomes."

About Coronary In-Stent Restenosis (ISR)
Coronary ISR is a serious complication of coronary stenting, which can increase the risk of life-threatening heart problems. It is characterized by re-narrowing of a coronary artery segment that was previously treated with a stent. According to the National Cardiovascular Data Registry, coronary ISR occurs in up to 10% of stented patients during the first year and continues at a rate of up to 3% per year thereafter, resulting in an estimated over 325,000 coronary ISR lesions annually worldwide that may require treatment. If left untreated, coronary ISR may lead to stable angina, unstable angina, acute coronary syndrome, acute myocardial infarction, or death.

About Virtue SAB
Virtue SAB is a highly differentiated, first-of-its-kind drug delivery angioplasty balloon system designed to deliver a proprietary extended-release formulation of sirolimus, SirolimusEFR™. It uses a patented non-coated microporous AngioInfusion™ Balloon to protect the drug in transit and consistently deliver a large liquid dose, overcoming certain limitations of drug-coated balloons. SirolimusEFR delivered by Virtue SAB has been shown in published preclinical series involving hundreds of arterial deliveries to achieve therapeutic levels of extended-release sirolimus through the critical healing period, exceeding published target tissue concentration of proven drug-eluting stents. Virtue SAB and SirolimusEFR demonstrated positive three-year clinical data in coronary ISR in the SABRE study, a multi-center, prospective, independent core lab-adjudicated clinical study of 50 patients conducted in Europe. Virtue SAB has been granted Breakthrough Device Designation by the FDA for the treatment of coronary ISR, coronary small vessel disease and below-the-knee peripheral artery disease.

About Orchestra BioMed

Orchestra BioMed is a biomedical innovation company accelerating high-impact technologies to patients through strategic collaborations with market-leading global medical device companies. The Company's two flagship product candidates - Atrioventricular Interval Modulation (AVIM) Therapy and Virtue® Sirolimus AngioInfusion™ Balloon (Virtue SAB) - are currently undergoing pivotal clinical trials for their lead indications, each representing multi-billion-dollar annual global market opportunities. AVIM Therapy is a bioelectronic treatment for hypertension, the leading risk factor for death worldwide, and is designed to be delivered as a firmware upgrade to a pacemaker and achieve immediate, substantial and sustained reductions in blood pressure in patients with hypertensive heart disease. The Company has a strategic collaboration with Medtronic (NYSE: MDT), one of the largest medical device companies in the world, for the development and commercialization of AVIM Therapy for the treatment of uncontrolled hypertension in pacemaker-indicated patients. AVIM Therapy has FDA Breakthrough Device Designation for these patients, as well as an estimated 7.7 million total patients in the U.S. with uncontrolled hypertension despite medical therapy and increased cardiovascular risk. Virtue SAB is a highly differentiated, first-of-its-kind drug delivery angioplasty balloon system designed to deliver a proprietary extended-release formulation of sirolimus, SirolimusEFR™, for the treatment of atherosclerotic artery disease, the leading cause of mortality worldwide. Virtue SAB has been granted Breakthrough Device Designation by the FDA for the treatment of coronary ISR, coronary small vessel disease and below-the-knee peripheral 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.

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 Virtue Trial, the ability of data from the Virtue Trial to support regulatory approval in the U.S., 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; 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 Annual Report on Form 10-K for the year ended December 31, 2024, which was filed with the Securities and Exchange Commission (the "SEC") on March 31, 2025, and the risk factor discussed under the heading "Item 1A. Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2025, which was filed with the SEC on May 12, 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.

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