Orchestra BioMed Receives FDA Approval of IDE to Initiate U.S. Coronary Pivotal Trial Randomizing First-in-Class Sirolimus-AngioInfusion Balloon, Virtue SAB, Head-to-Head with Paclitaxel-Coated Balloon

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- *Orchestra BioMed's Virtue® Sirolimus AngioInfusion Balloon™ ("Virtue SAB") is the only non-coated drug-eluting balloon system under clinical investigation worldwide and has been awarded multiple FDA Breakthrough Device Designations*
- *The Virtue Trial will be the first U.S. IDE head-to-head randomized evaluation of a sirolimus-eluting balloon versus a commercially available paclitaxel-coated balloon (AGENT™) for the treatment of coronary in-stent restenosis ("ISR")*
- *Robust non-inferiority trial is designed to provide a clear pathway to regulatory approval as well as potentially showcase clinical advantages of Virtue SAB*
- *With the amended IDE approved by the FDA, Orchestra BioMed is currently targeting initiation of the Virtue Trial during the second half of 2025*

NEW HOPE, Pa., April 29, 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 that the U.S. Food and Drug Administration ("FDA") has approved its Investigational Device Exemption ("IDE") amendment to initiate an updated design of the Company's planned *Virtue SAB in the Treatment of Coronary ISR Trial* ("Virtue Trial"). The IDE provides FDA regulatory clearance for Orchestra BioMed to initiate a U.S. pivotal clinical trial comparing its highly differentiated, next-generation Sirolimus-AngioInfusion Balloon, Virtue SAB to the Boston Scientific AGENT paclitaxel-coated balloon, currently the only drug-coated balloon ("DCB") FDA-approved for a coronary indication. Data from the Virtue Trial will be used to support regulatory approval in the U.S. Virtue SAB and SirolimusEFR are investigational technologies owned by Orchestra BioMed, which also controls and is responsible for all regulatory filings, clinical operations, and drug and device supplies for the Virtue Trial.

The Differentiation of Virtue SAB, An FDA Breakthrough Designated Device
Virtue SAB is designed to deliver a proprietary extended-release formulation of sirolimus, SirolimusEFR™, through a non-coated microporous AngioInfusion™ Balloon that protects the drug in transit to consistently deliver a large liquid dose, overcoming certain limitations of DCBs. SirolimusEFR™ enables tissue uptake and extended release of the required therapeutic levels of sirolimus (> 1ng/mg tissue concentration), the "gold-standard" drug for preventing arterial restenosis, through the critical healing period of approximately 30 days. Virtue SAB has been previously granted FDA Breakthrough Device Designation for the treatment of coronary ISR as well as for coronary small vessel disease and peripheral artery disease below-the-knee. In the multi-center SABRE pilot study, Virtue SAB demonstrated best-in-class clinical results for the treatment of coronary ISR, including 12-month target lesion failure of 2.8% and 6-month late lumen loss of 0.12mm.

"Virtue SAB has the potential to be one of the most compelling technologies in interventional cardiology. It's the only product in development that optimizes both the arterial tissue uptake and retention of sirolimus to achieve pharmacokinetics that match or even exceed those of proven 'limus-eluting stents," said Dean J. Kereiakes, M.D., FACC, MSCAI, Chairman of The Christ Hospital Heart & Vascular Institute, Medical Director of The Christ Hospital Research Institute, Professor of Clinical Medicine at The Ohio State University, Professor of Medicine at University of Cincinnati and Co-Principal Investigator on the Virtue Trial.

Dr. Kereiakes continued: "Virtue SAB is designed to consistently deliver a large liquid dose of an extended-release formulation of sirolimus to overcome certain limitations of traditional DCBs, including lower doses due to surface area and coating integrity constraints, drug loss in transit leading to inconsistent dosing, and the risk of emboli from large coating particulates. As the coronary treatment landscape continues to shift toward more rapid adoption of DCBs, I'm excited about the potential of Virtue SAB to set a new standard of care."

"Drug-coated balloons are emerging as a new standard of care in the treatment of various coronary and peripheral indications, and I believe utilization of this class of technology will continue to grow and evolve over time as the science is expanding. In a field largely reliant on paclitaxel drug-coated balloons, Virtue SAB stands out as the only device with a completely different mechanism of action; namely to provide delivery of a large liquid dose of an extended-release formulation sirolimus," commented Allen Jeremias, MD, MSc, Associate Director of the Cardiac Catheterization Laboratory at St. Francis Hospital & Heart Center, and Co-Principal Investigator on the Virtue Trial. "Having had the opportunity to work with several DCBs, I anticipate continued momentum for this class, and am eager to see how Virtue SAB, particularly with its anti-restenotic, anti-inflammatory and cytostatic SirolimusEFR formulation, performs in a head-to-head trial against a paclitaxel-coated balloon."

Showcasing Distinctive and Sustainable Advantages of Virtue SAB Through a Head-to-Head Trial

"We believe there is a multibillion-dollar U.S. market for coronary drug delivery balloons based on the significant unmet clinical need, market demand, and established reimbursement," said David Hochman, Chairman and Chief Executive Officer of Orchestra BioMed. "We made a deliberate, strategic decision to pursue a head-to-head trial with the commercially available AGENT paclitaxel-coated balloon, underscoring our confidence in Virtue SAB as a fundamentally differentiated solution for the treatment of atherosclerosis. We believe this approach offers the most direct path to regulatory approval while also providing the best opportunity to demonstrate what we believe are distinctive and sustainable advantages of our proprietary technology."

Mr. Hochman continued, "The superior safety and efficacy of sirolimus over paclitaxel was made clear by the performance of drug-eluting stents. Published meta-analysis involving 76 trials show 'limus-eluting stents have significantly better clinical performance than paclitaxel-eluting stents in terms of target lesion revascularization and major adverse cardiac events.[1] We believe this is due to their ability to maintain sufficient drug tissue concentration through the critical healing period of approximately 30 days, because stents that failed to do this did not perform well clinically.[2,3,4] Virtue SAB is the only drug delivery balloon that has demonstrated comparable drug tissue levels to clinically successful drug-eluting stents in large published preclinical studies, without the need to leave a permanent metal implant in the artery. Our pilot clinical results with Virtue SAB also highlight the potential for optimal clinical outcomes with robust sirolimus delivery. We're excited to showcase the full potential of Virtue SAB in this landmark trial and are proud of our team and grateful to our clinical collaborators for their work in achieving this important milestone."

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, a difficult-to-treat and serious complication of coronary stenting. 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 will randomize 740 patients across up to 75 centers in the U.S. With the amended IDE approved by the FDA, Orchestra BioMed is currently targeting initiation of the Virtue Trial during the second half of 2025, bringing the Company one step closer to delivering a next-generation solution for atherosclerotic disease.

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 a 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 designed to deliver a proprietary extended-release formulation of sirolimus, SirolimusEFR™ through a non-coated microporous AngioInfusion™ Balloon that protects the drug in transit to 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 sustained tissue levels well above the known required therapeutic tissue concentration for inhibiting restenosis (1 ng/mg tissue) for the entire critical healing period of approximately 30 days. Virtue SAB 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 specific indications relating to coronary ISR, coronary small vessel disease and peripheral artery disease below-the-knee.

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 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. The company has received four Breakthrough Device Designations from the U.S. FDA across these two core programs, reflecting the significant potential of its technologies to address high unmet needs in cardiovascular care. 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 timing of the initiation and of the Virtue Trial, the number of patients to be enrolled in the Virtue Trial, and the potential safety and efficacy of the Company's product candidates, including the ability of Virtue SAB to overcome certain limitations of DCBs. 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; 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 filed with the U.S. 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.

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