Source: *Orchestra BioMed Holdings, Inc.*

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Ligand and Medtronic Commit $70 Million in Strategic Capital to Orchestra BioMed

• Ligand to invest $35 million in exchange for a tiered royalty on future sales of Orchestra's AVIM therapy and Virtue SAB and an additional $5 million in an equity private placement

• Medtronic to invest $10 million in an equity private placement and an additional $20 million in a secured subordinated promissory note convertible to prepaid revenue share

• Medtronic and Orchestra BioMed expand strategic collaboration to provide pathway for development of AVIM therapy-enabled leadless pacemakers

NEW HOPE, Pa., July 31, 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 Company has secured $70 million in new capital from Ligand Pharmaceuticals Incorporated (Nasdaq: LGND, "Ligand") and Medtronic, plc. (NYSE: MDT, "Medtronic") to advance its late-stage partnered cardiology programs.

Simultaneously, Orchestra BioMed and Medtronic, which have an existing strategic collaboration for atrioventricular interval modulation ("AVIM") therapy for the treatment of uncontrolled hypertension in pacemaker-indicated patients, have amended their agreement to include the potential future development of AVIM therapy-enabled leadless pacemakers. Unlike traditional pacemakers that are placed in a patient's chest with leads (or wires) running to the heart, minimally-invasive Medtronic Micra™ leadless pacemakers are implanted directly into the heart, reducing potential sources of complications.

Ligand $40 million Investment

Todd Davis, Chief Executive Officer of Ligand commented: "We are pleased to partner with Medtronic and Orchestra BioMed in this important endeavor. This investment expands our pipeline of development-stage products and demonstrates our confidence in Orchestra BioMed's scientific advancements, as well as the strong capabilities of its partner, Medtronic. We are proud to support Orchestra BioMed as they develop novel high-impact, device-based therapies such as AVIM therapy and Virtue SAB targeting high-risk patient populations with hypertension and arterial disease, two of the most significant global health challenges."

David Hochman, Chairman and Chief Executive Officer of Orchestra BioMed stated, "Ligand has been one of the inspirations for our partnership-driven approach to creating long-term, capital-efficient value through royalty-based collaborations. We are thrilled to welcome them as a strategic capital partner. Ligand's decision to invest in our partnered programs and our team reflects our shared conviction in the transformative potential of both AVIM therapy and Virtue SAB – our late-stage flagship technologies aimed to address important unmet medical needs in large, established global markets. This transaction provides foundational financial support to enable our potential achievement of key value creating milestones for both of our high-impact clinical programs."

Under the terms of the agreement, Ligand will pay $20 million to Orchestra BioMed at closing with an additional $15 million to be funded, subject to certain conditions precedent, at the nine-month anniversary of the transaction closing date. Ligand has also agreed to invest an additional $5 million to purchase shares of the Company's common stock in an equity private placement at the public offering price per share in Orchestra BioMed's next public offering of its equity securities. In exchange, Ligand will receive a low double-digit royalty on the first $100 million in commercial revenues from Orchestra's AVIM therapy and Virtue SAB programs in all indications. Ligand will also earn a mid-single-digit royalty on annual revenues exceeding $100 million in commercial revenues from AVIM therapy in the uncontrolled hypertension and increased cardiovascular risk indication and Virtue SAB in coronary artery disease indications.

Medtronic $30 million Additional Investment & Future Leadless AVIM Therapy Device Development

Robert C. Kowal, M.D., Ph.D., Vice President and General Manager of Cardiac Pacing Therapies within the Medtronic Cardiac Rhythm Management operating unit, commented: "Our expanded investment in Orchestra BioMed reflects confidence in their clinical progress. Broadening our collaboration to include integrating AVIM therapy into future leadless pacing technology reaffirms our commitment to transform care for patients who need pacing therapy and have uncontrolled hypertension."

Mr. Hochman added, "Medtronic continues to be an outstanding partner for the AVIM therapy program. We believe their $30 million additional commitment to Orchestra BioMed reflects their belief in the clinical and commercial potential for this therapy to benefit patients with uncontrolled hypertension and increased cardiovascular risk in the pacemaker population. Expanding our existing collaboration to provide for potential future integration of AVIM therapy into a leadless pacemaker system deepens our strategic alignment and creates a potential pathway for patients to benefit from both AVIM therapy and cutting-edge leadless pacing technology, simultaneously."

Subject to the terms of the agreement, Medtronic's $30 million additional investment commitment to Orchestra BioMed includes a $10 million agreement to purchase shares of the Company's common stock in a private placement at the public offering price in the Company's next public offering of its equity securities. Medtronic also made a $20 million commitment to purchase a five-year term secured subordinated promissory note, to be funded in nine months which automatically converts to a prepaid revenue share upon U.S. Food and Drug Administration ("FDA") approval of AVIM therapy. The prepaid revenue share will be credited back to Medtronic at a low double-digit percentage of actual AVIM therapy revenue share paid to Orchestra BioMed, up to $40 million in cumulative revenue share.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company enabling scientific advancement through supporting the clinical development of high-value medicines. Ligand does this by providing financing, licensing our technologies or both. Ligand's business model seeks to generate value for stockholders by creating a diversified portfolio of biotech and pharmaceutical product revenue streams that are supported by an efficient and low corporate cost structure. Ligand's goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable and diversified manner. Ligand's business model is based on funding programs in mid- to late-stage drug development in return for economic rights, purchasing royalty rights in development stage or commercial biopharmaceutical products and licensing its technology to help partners discover and develop medicines. Ligand partners with other pharmaceutical companies to attempt to leverage what they do best (late-stage development, regulatory management and commercialization) in order to generate revenue. Ligand operates two infrastructure-light royalty generating technology IP platform technologies. Ligand's Captisol® platform technology is a chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Ligand's NITRICIL™ platform technology

facilitates tunable dosing, permitting an adjustable drug release profile to allow proprietary formulations that target a broad range of indications. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Jazz, Gilead Sciences and Baxter International. For more information, please visit www.ligand.com. Follow Ligand on X and LinkedIn.

Ligand uses its investor relations website and X as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Investors should monitor our website and our X account, in addition to following our press releases, SEC filings, public conference calls and webcasts.

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 AVIM therapy for the treatment of hypertension, the leading risk factor for death worldwide. Orchestra BioMed is also developing Virtue 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 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.

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 further 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.

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.

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, implementation and design of the Company's planned and ongoing pivotal trials, realizing the clinical and commercial value of the Company's product candidates, the potential safety and efficacy of the Company's product candidates, the ability of the Company's partnerships to accelerate clinical development, and the Company's ability to satisfy funding and closing conditions of the transactions described in this press release. 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 commercial 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 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.

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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