LivaNova Provides Update on RECOVER Clinical Study Evaluating VNS Therapy for Treatment-Resistant Depression in Unipolar Patients

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Primary endpoint did not achieve statistical significance in unipolar patient cohort

Statistically significant and clinically meaningful benefits seen in select secondary endpoints; no safety concerns identified

LONDON--(BUSINESS WIRE)--Jun. 6, 2024-- LivaNova PLC (Nasdaq: LIVN), a market-leading medical technology company, today announced the preliminary results for the unipolar patient cohort of the RECOVER clinical study, assessing the use of VNS Therapy™ in treatment-resistant depression. The study did not meet its primary endpoint (PE) for the unipolar cohort; however, statistical significance was achieved in select secondary endpoints.

The PE measured the difference between active and sham VNS Therapy on the rate of Montgomery–Åsberg Depression Rating Scale (MADRS) response for the unipolar patient cohort with a predetermined p-value of $p<0.023$. Over the course of 12 months, the active treatment arm demonstrated statistically significant and clinically meaningful improvement from the treatment arm's baseline. Due to a strong response in the sham group, which was unforeseen in the study design, statistical separation between the treatment and sham arms for the PE was not achieved by the end of the study. Despite this, the totality of data supports a meaningful treatment effect for those who received active VNS Therapy particularly given that the RECOVER unipolar patient population has a significant unmet need after having failed numerous other treatment modalities.

"We would like to thank the patients and physicians who participated in RECOVER to date, as well as the U.S. Centers for Medicare and Medicaid Services, who we partnered with to design this study," said Vladimir Makatsaria, Chief Executive Officer of LivaNova. "Despite not achieving statistical significance for the primary endpoint for the unipolar cohort in the RECOVER study, the effect of active VNS Therapy was within our expectations and resulted in clinically meaningful benefits in select secondary endpoints. We are conducting an in-depth analysis of the data with key stakeholders and will determine the path forward in the coming weeks."

The Company expects to publish the unipolar cohort data, including details on the PE and secondary endpoints, in peer-reviewed journals in the fourth quarter of 2024. Importantly, no safety issues were reported.

"I am encouraged by the clinically meaningful outcomes for the RECOVER unipolar patient population that is markedly treatment resistant," said Dr. Charles R. Conway, Director of the Washington University in St. Louis Resistant Mood Disorders Center and Principal Investigator for RECOVER. "As we have previously published, the unipolar patients who entered the RECOVER study were of a greater severity than we had anticipated in the study design and have very few treatment options remaining. We now have a large body of data to evaluate, and I look forward to better understanding it in totality."

The bipolar patient cohort continues for RECOVER and LivaNova will continue its discussions with the U.S. Centers for Medicare and Medicaid Services (CMS) regarding reconsideration of coverage for VNS Therapy for treatment-resistant depression.

About RECOVER

LivaNova's VNS Therapy has been approved for the treatment of depression since earning CE Mark in 2001 and 510(k) from the U.S. Food and Drug Administration in 2005. RECOVER – which stands for A **P**rospective, Multi-c**e**nter, Randomized **C**ontrolled Blinded Trial Dem**o**nstrating the Safety and Effectiveness of **V**NS Therapy™ System as Adjunctiv**e** Therapy Versus a No Stimulation Control in Subjects With Treatment-**R**esistant Depression – is a clinical study initiated in September 2019 as part of a Coverage with Evidence Development framework per the U.S. Centers for Medicare and Medicaid (CMS) National Coverage Determination process.

The largest randomized clinical study of its kind, RECOVER is examining up to 1,000 patients ages 18 or older who have unipolar or bipolar depression that is difficult to treat. The double-blind, randomized controlled study is assessing how VNS Therapy can offer patients relief from their depressive symptoms and improve quality of life. It is being carried out at up to 100 leading hospitals and medical centers across the United States. For more information on the RECOVER clinical study, please visit www.RECOVERVNS.com.

About VNS Therapy for Depression

The VNS Therapy™ System, Symmetry™, is FDA approved and indicated in the U.S. for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments. Commonly reported side effects are hoarseness, shortness of breath, sore throat and coughing. Side effects typically occur during stimulation and are less noticeable over time. Safety information is available here.

About LivaNova

LivaNova PLC is a global medical technology company built on nearly five decades of experience and a relentless commitment to provide hope for patients and their families through medical technologies, delivering life-changing solutions in select neurological and cardiac conditions. Headquartered in London, LivaNova employs approximately 2,900 employees and has a presence in more than 100 countries for the benefit of patients, healthcare professionals and healthcare systems worldwide. For more information, please visit www.livanova.com.

Safe Harbor Statement

This news release contains "forward-looking statements" concerning the Company's goals, beliefs, expectations, strategies, objectives, plans, underlying assumptions and other statements that are not necessarily based on historical facts. These statements include, but are not limited to, statements regarding progress relating to the RECOVER study and the VNS Therapy System, Symmetry. Actual events may differ materially from those indicated in our forward-looking statements as a result of various factors, including those factors set forth in Item 1A of the Company's most

recent Annual Report on Form 10-K, as supplemented by any risk factors contained in Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. LivaNova undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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