Wave Life Sciences Announces Initiation of Dosing in Phase 2 FORWARD-53 Trial of WVE-N531 in Duchenne Muscular Dystrophy

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FORWARD-53 is fully enrolled with potentially registrational dystrophin expression data expected in 2024

Previous clinical proof-of-concept data demonstrated highest level of exon skipping ever observed in the clinic and that WVE-N531 was present in myogenic stem cells, which are important for potential muscle regeneration

CAMBRIDGE, Mass., Dec. 15, 2023 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced the initiation of dosing in the Phase 2 FORWARD-53 clinical trial, which is evaluating WVE-N531 as a treatment for boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 53 skipping. FORWARD-53 is designed to assess functional dystrophin protein at 24 and 48 weeks with every other week dosing of WVE-N531.

“Following encouraging data from the WVE-N531 proof-of-concept trial, we believe we are on the right path toward addressing a significant unmet need in DMD – the generation of endogenous dystrophin protein to levels that meaningfully impact the trajectory of the disease,” said Anne-Marie Li-Kwai-Cheung, MChem, MTOPRA, RAPS, Chief Development Officer at Wave Life Sciences. “Our clinical data in boys with DMD amenable to exon 53 skipping demonstrated the highest level of exon skipping ever observed in the clinic, and high muscle concentrations of WVE-N531 in skeletal muscle of 6.1 micromolar. Importantly, in our non-human primate studies, muscle concentrations were higher in the diaphragm and heart than in skeletal muscle. Additionally, while FORWARD-53 is dosing every other week, we have the potential for monthly dosing in the future. For these reasons, we are excited about the potential of WVE-N531. We are grateful to the DMD community for their continued support and look forward to announcing dystrophin expression data in 2024, as well as advancing exon skipping candidates for other mutations if FORWARD-53 is successful.”

FORWARD-53 is a potentially registrational, open-label, Phase 2 clinical trial that has enrolled 10 boys with DMD who are amenable to exon 53 skipping. The trial is powered to evaluate functional, endogenous dystrophin expression following 24 and 48 weeks of every other week, intravenous dosing at 10 mg/kg. The primary endpoint is dystrophin protein levels, and the trial is also evaluating pharmacokinetics, digital and functional endpoints, and safety and tolerability.

FORWARD-53 is fully enrolled, and Wave expects to deliver data, including dystrophin expression from muscle biopsies, in 2024.

Wave’s Phase 1b/2a Part A proof-of-concept trial in boys with DMD amenable to exon 53 skipping demonstrated high muscle concentrations of WVE-N531 (mean of 6.1 micromolar or 42 micrograms/gram) and mean exon skipping of 53% (range: 48-62%) at six weeks, after boys received three doses of 10 mg/kg every other week. WVE-N531 appeared safe and well-tolerated, with all treatment-related adverse events being mild.

Additionally, at Wave’s R&D Day in September 2023, the company shared an analysis of muscle biopsy data from the Part A proof-of-concept trial indicating that WVE-N531 was present in myogenic stem cells, which are important for potential muscle regeneration. These are the first clinical data in DMD to demonstrate uptake in myogenic stem cells at the early, six-week timepoint and further support the potential differentiation of WVE-N531 from other therapeutics, including gene therapies.

About Duchenne Muscular Dystrophy
Duchenne muscular dystrophy (DMD) is a fatal X-linked genetic neuromuscular disorder caused predominantly by out-of-frame deletions in the dystrophin gene, resulting in absent or defective dystrophin protein. Dystrophin protein is needed for normal muscle maintenance and operation. Because of the genetic mutations in DMD, the body cannot produce functional dystrophin, which results in progressive and irreversible loss of muscle function, including the heart and lungs. Worldwide, DMD affects approximately one in 5,000 newborn boys. Approximately 8%-10% of DMD patients have mutations amenable to treatment with an exon 53 skipping therapy. Exon skipping aims to address the underlying cause of DMD by promoting the production of dystrophin protein to stabilize or slow disease progression.

About Wave Life Sciences
Wave Life Sciences (Nasdaq: WVE) is a clinical-stage RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases. Wave aspires to develop best-in-class medicines across multiple therapeutic modalities using PRISM, the company’s proprietary discovery and drug development platform that enables the precise design, optimization, and production of stereopure oligonucleotides. Driven by a resolute sense of urgency, the Wave team is targeting a broad range of genetically defined diseases so that patients and families may realize a brighter future. To find out more, please visit www.wavelifesciences.com and follow Wave on X (formerly Twitter) @WaveLifeSci.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, our understanding of the anticipated therapeutic benefit of WVE-N531 as a therapy for DMD; our expectations for our FORWARD-53 clinical trial and potential registration; our understanding of the cause of DMD and the potential addressable patients amenable to treatment with an exon 53 skipping therapy; our expectation that the generation of endogenous dystrophin protein will have a positive impact on patients with DMD; our expectations and anticipated timing for delivering dystrophin data, including muscle biopsies, in DMD patients treated with WVE-N531; our expectations for advancing exon skipping candidates for other mutations in DMD; and the potential benefits of PRISM, including our novel PN backbone chemistry modifications, and our stereopure oligonucleotides compared with stereorandom oligonucleotides. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release and actual results may differ materially from those indicated by these forward-looking statements as a result of these risks, uncertainties and important factors, including, without limitation, the risks and uncertainties described in the section entitled “Risk Factors” in Wave’s most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as amended, and in other filings Wave makes with the SEC from time to time. Wave undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstance.

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