Wave Life Sciences Receives FDA Rare Pediatric Disease Designation for WVE-N531 for the Treatment of Duchenne Muscular Dystrophy

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Designation highlights significant unmet needs in DMD; dystrophin data from potentially registrational FORWARD-53 trial of WVE-N531 are on track for 3Q 2024

In previous Part A trial, WVE-N531 achieved industry-leading exon skipping of 53% and muscle tissue concentrations that were approximately 20-30 times higher than those reported by exon skipping technologies leveraging muscle delivery conjugates

CAMBRIDGE, Mass., Aug. 12, 2024 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health, today announced that the U.S. Food and Drug Administration (FDA) has granted Rare Pediatric Disease Designation to WVE-N531 for the treatment of boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 53 skipping. WVE-N531 is currently being evaluated in the potentially registrational FORWARD-53 clinical trial and Wave expects to deliver data, including dystrophin protein expression from muscle biopsies after 24 weeks of treatment, in the third quarter of 2024.

"This designation from FDA underscores that significant unmet needs remain in DMD, and it also supports Wave's innovative and purposeful approach to drug development in the rare disease space," said Anne-Marie Li-Kwai-Cheung, MChem, MTOPRA, RAPS, Chief Development Officer at Wave Life Sciences. "With our WVE-N531 program, we are aiming to restore clinically meaningful levels of near full length, functional dystrophin protein. Positive data from FORWARD-53 would also unlock additional programs for other exons in our pipeline, with the goal of developing best-in-class medicines that address the underlying cause of the disease for up to 40% of boys with DMD."

WVE-N531 is an exon skipping oligonucleotide designed to induce production of endogenous, functional dystrophin protein. In the previously completed Part A study (three 10 mg/kg doses every other week), WVE-N531 achieved industry-leading mean exon skipping levels of 53% and mean muscle tissue concentrations of ~42,000 ng/g (~6,100 nM), which is approximately 20-30 times higher than levels reported by exon-skipping technologies leveraging muscle delivery conjugates in DMD patients. The Part A data also demonstrated distribution to myogenic stem cells (also known as satellite cells) in all study participants. Myogenic stem cells are progenitor cells for new myoblasts, and Wave is not aware of any other clinical data for exon skipping therapies or gene therapies that have demonstrated myogenic stem cell uptake. Preclinical data in non-human primates also demonstrated concentrations of WVE-N531 in the heart and diaphragm that exceeded skeletal muscle, which indicates the potential for WVE-N531 to also offer cardiac and respiratory benefits.

WVE-N531 is currently being investigated in FORWARD-53, a potentially registrational, open-label clinical trial in 11 boys with DMD. Endpoints include dystrophin expression after 24 and 48 weeks of treatment, as well as pharmacokinetic, safety and tolerability data.

Rare Pediatric Disease Designation is granted by the FDA for serious or life-threatening diseases which primarily affect individuals less than 18 years of age and fewer than 200,000 people in the United States. If a New Drug Application for WVE-N531 is approved by the FDA, Wave would be eligible to receive a Priority Review Voucher.

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 biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health. Wave's RNA medicines platform, PRISM ®, combines multiple modalities, chemistry innovation and deep insights in human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Its toolkit of RNA-targeting modalities includes editing, splicing, RNA interference and antisense silencing, providing Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's diversified pipeline includes clinical programs in Duchenne muscular dystrophy, Alpha-1 antitrypsin deficiency and Huntington's disease, as well as a preclinical program in obesity. Driven by the calling to "Reimagine Possible", Wave is leading the charge toward a world in which human potential is no longer hindered by the burden of disease. Wave is headquartered in Cambridge, MA. For more information on Wave's science, pipeline and people, please visit www.wavelifesciences.com and follow Wave on X (formerly Twitter) and LinkedIn.

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, the potential significance and implications of receiving the Rare Pediatric Disease Designation from the FDA; the potentially registrational nature of our FORWARD-53 trial for WVE-N531; our expectations that WVE-N531's industry-leading exon skipping and muscle tissue concentrations has the potential to become the leading exon-skipping therapeutic in DMD; our expectations that high tissue concentrations and high exon skipping may result in high dystrophin restoration following a sufficient follow up period; our understanding of the importance of satellite cells for muscle regeneration; our expectation that WVE-N531 muscle concentrations in the clinic may be higher in heart and diaphragm than in skeletal muscle; and our expectations of the anticipated therapeutic benefits of WVE-N531 for DMD over existing therapies. 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 circumstances.

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