Wave Life Sciences Announces Initiation of Dosing in Phase 1b/2a Clinical Trial of WVE-N531 in Duchenne Muscular Dystrophy

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Trial is expected to enroll 15 boys with DMD amenable to exon 53 skipping

First systemically administered therapeutic candidate with PN backbone chemistry modifications to be assessed in the clinic

Preclinical in vivo data with PN backbone chemistry modified-exon skipping compounds showed significant improvement of survival and dystrophin expression in mice compared with compounds designed with Wave's first-generation chemistry

Clinical data to enable decision-making on next steps for WVE-N531 to be generated through 2022

CAMBRIDGE, Mass., Sept. 29, 2021 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced the initiation of dosing in a Phase 1b/2a clinical trial evaluating investigational WVE-N531 as a treatment for boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 53 skipping. WVE-N531 is Wave's first exon skipping candidate, and the first candidate systemically administered by intravenous infusion, to utilize its novel PN backbone chemistry modifications (PN chemistry).

"There remains a significant unmet need for DMD treatments that restore sufficient functional dystrophin protein in muscle, thus addressing the underlying cause of disease in a way that likely establishes clinical benefit," said Michael Panzara, MD, MPH, Chief Medical Officer and Head of Therapeutics Discovery and Development at Wave Life Sciences. "Our preclinical data suggest that the incorporation of PN chemistry into WVE-N531 has the potential to overcome the issues of poor intracellular access often seen with exon-skipping approaches to DMD, including our prior clinical program. We expect to generate clinical data through 2022 that will enable decision-making on further development of WVE-N531, as well as other PN-modified exon skipping compounds."

A preclinical study of WVE-N531 demonstrated a dose-dependent increase in dystrophin production of up to 71% in DMD patient-derived myoblasts (precursors to muscle cells) *in vitro*. Additionally, preclinical studies in double knockout mice, a severe and rapidly fatal *in vivo* model lacking both dystrophin and utrophin protein, showed that treatment with PN chemistry-modified compounds resulted in 100% survival at the time of study termination (~40 weeks) as compared to a median survival of less than 12 weeks for mice treated with compounds designed with Wave's first-generation chemistry. Further, bi-weekly dosing is supported by higher concentrations and broader distribution in non-human primates with WVE-N531 as compared to Wave's first-generation compound.

The open-label Phase 1b/2a study is evaluating the safety and tolerability of ascending doses of WVE-N531. Additional objectives of the study include pharmacokinetics (muscle concentration) and pharmacodynamics (dystrophin expression). The study is expected to enroll 15 boys with DMD ages 5 to 12 years who have a documented mutation in the dystrophin gene that is amenable to exon 53 skipping and are ambulatory or non-ambulatory. Up to four dose levels of WVE-N531 will be evaluated in order to select a dose for further multidose evaluation, administered as a bi-weekly infusion.

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 genetic 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 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, the anticipated therapeutic benefit of WVE-N531 as a therapy for DMD; expected patient enrollment in the Phase 1b/2a Clinical Trial of WVE-N531 trial; our beliefs regarding the learnings gained from our first-generation chemistry and clinical programs; the anticipated timing of data to enable decision-making on next steps for WVE-N531 and other PN-modified exon skipping compounds; our understanding of how the incorporation of PN chemistry into WVE-N531 may improve potential therapies for DMD; the predicted pharmacology of WVE- N531 and the associated trial protocol, design and endpoints; our understanding of the cause of DMD and the potential addressable patients amenable to treatment with an exon 53 skipping therapy; the anticipated therapeutic benefits of our potential therapies, including our compounds containing PN chemistry; and the potential benefits of PRISM, including our stereopure 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 circumstances.

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