



Wave Life Sciences Duchenne Muscular Dystrophy Clinical Trial Selected for FDA Complex Innovative Trial Designs Pilot Program

January 3, 2019

Suvodirsen (WVE-210201) Phase 2/3 trial chosen in inaugural round of pilot program

FDA pilot program is a 21st Century Cures Act initiative

CAMBRIDGE, Mass., Jan. 03, 2019 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (NASDAQ: WVE), a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases, today announced that the planned Phase 2/3 efficacy and safety trial for its lead Duchenne muscular dystrophy (DMD) clinical program has been selected for the U.S. Food and Drug Administration (FDA) pilot program for complex innovative trial designs (CID). The selection was based on the design of Wave's Phase 2/3 clinical trial of suvodirsen (WVE-210201), an investigational therapy for boys with DMD who are amenable to exon 51 skipping. This marks the first time that the FDA has selected clinical protocols for its CID pilot program that was announced in August 2018.

In evaluating submissions for the CID pilot program, the FDA considered two key criteria: the innovative features of the trial design and the therapeutic need (i.e., therapies being developed for use in disease areas where there are limited or no treatment options). Wave's application for the CID pilot program includes a plan to leverage DMD historical control data to augment the placebo arm of the suvodirsen Phase 2/3 clinical trial, among other innovative design elements. Through this pilot program, Wave intends to reduce the number of patients required to deliver conclusive clinical efficacy results, thereby minimizing the number of patients required in the placebo treatment arm and potentially accelerating study completion. As a participant in the pilot program, the company will also have additional opportunities to meet with FDA staff to discuss the design elements of the trial, including the use of Bayesian methods to adapt the trial and allow for more efficient and productive clinical determinations. Details of Wave's Phase 2/3 trial design will be presented at upcoming scientific meetings.

"In designing our clinical trials, we are constantly looking to maximize the probability of a definitive result, incorporate the feedback of patients and their families, and reduce the burden on those who are already bravely enduring the challenges associated with serious, genetically-defined diseases. The FDA's recognition of our plan reflects the thoughtful and collaborative way in which we approach clinical development," said Michael Panzara, MD, MPH, Chief Medical Officer of Wave Life Sciences. "We look forward to further discussions with the FDA in the coming months and sharing learnings from our trial design with others in the rare disease drug development community to drive greater efficiency and productivity in future clinical studies."

Wave anticipates initiating the global, placebo-controlled Phase 2/3 efficacy and safety clinical trial of suvodirsen in DMD patients amenable to exon 51 skipping in 2019. The trial is designed to measure clinical efficacy and dystrophin expression, and Wave intends to use the results of this trial to seek regulatory approvals globally. Currently, suvodirsen is being studied in an ongoing open-label extension (OLE) study and Wave expects to deliver an interim analysis of dystrophin expression from this study in the second half of 2019.

The FDA CID pilot program is an initiative under the 21st Century Cures Act, with an objective to modernize clinical trial design, help streamline and advance drug development and inform easier regulatory decision-making. In order to qualify for the CID pilot program, companies must intend to provide substantial evidence of efficacy through a complex, novel design that incorporates innovative trial design elements such as seamless trial designs, modeling and simulations to assess trial operating characteristics, the use of biomarker enriched populations, complex adaptive designs, Bayesian models and other benefit-risk determinations, among others. For more information, visit <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm617212.htm>.

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. Globally, DMD affects approximately one in 5,000 newborn boys.

About Suvodirsen (WVE-210201)

Suvodirsen is an investigational stereopure oligonucleotide that has been shown to induce skipping of exon 51 of *dystrophin* pre-mRNA in preclinical studies and is intended for the treatment of Duchenne muscular dystrophy (DMD). Approximately 13% of DMD patients have genetic mutations that are amenable to treatment with an exon 51 skipping therapy. Exon-skipping technology has the potential to induce cellular machinery to 'skip over' a targeted exon and restore the reading frame, resulting in the production of internally truncated, but functional dystrophin protein. Wave preclinical *in vitro* experiments using gymnotic delivery (free uptake) of suvodirsen in DMD patient-derived myoblasts demonstrated efficient exon 51 skipping and dystrophin protein restoration. Preclinical Western blot studies of suvodirsen demonstrated 52% dystrophin protein restoration compared with normal skeletal muscle tissue lysates. Suvodirsen has been granted orphan drug designation for the treatment of DMD by the U.S. Food and Drug Administration (FDA) and the European Commission, as well as rare pediatric disease designation by the FDA.

About Suvodirsen (WVE-210201) Clinical Trials

Suvodirsen is being studied in a global, multicenter, double-blind, placebo-controlled Phase 1 clinical trial designed to evaluate the safety, tolerability and plasma concentrations of single ascending doses of suvodirsen administered intravenously in Duchenne muscular dystrophy patients with gene mutations amenable to exon 51 skipping. The trial is expected to enroll up to 40 patients, including ambulatory and non-ambulatory patients between 5 and 18 years of age. In December 2018, the company announced that, based on results from four ascending dose cohorts in the Phase 1 clinical trial, the safety and tolerability profile of suvodirsen supports initiation of a Phase 2/3 clinical trial.

As patients complete the Phase 1 trial, they have the option to enroll in an ongoing open-label extension (OLE) study in which they receive suvodirsen. The company remains on track to deliver an interim analysis of dystrophin expression from muscle biopsies in boys receiving suvodirsen in the OLE study in the second half of 2019. Data from this analysis are intended to be an important component of a submission to the U.S. Food and Drug Administration for accelerated approval in the United States.

About Wave Life Sciences

Wave Life Sciences is a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases. Its chemistry platform enables the creation of highly specific, well characterized oligonucleotides designed to deliver superior efficacy and safety across multiple therapeutic modalities. The company's pipeline is initially focused on neurological disorders and extends across several other therapeutic areas. For more information, please visit www.wavelifesciences.com and follow Wave on Twitter [@WaveLifeSci](https://twitter.com/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 potential benefits of being selected to participate in the FDA's pilot program for complex innovative trial designs, the expected timing of initiation of a suvodirsen Phase 2/3 clinical trial, the plans to present details of the suvodirsen Phase 2/3 trial design at upcoming scientific meetings, the expected timing of an interim analysis of dystrophin expression from muscle biopsies in boys receiving suvodirsen in the OLE study, and Wave's intention to use the results of the Phase 2/3 trial to seek regulatory approvals globally. 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, 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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Source: Wave Life Sciences