Wave Life Sciences Announces Suvodirsen Phase 1 Safety and Tolerability Data and Phase 2/3 Clinical Trial Design

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Data to be presented today at 2019 Muscular Dystrophy Association Clinical and Scientific Conference

Phase 2/3 clinical trial for suvodirsen in DMD expected to initiate in July 2019

Interim efficacy data from ongoing open-label extension study expected in H2 2019

Investor conference call scheduled for 7:30 a.m. ET today to discuss Phase 1 results and Phase 2/3 trial design

CAMBRIDGE, Mass., April 16, 2019 (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 final results from its Phase 1 clinical trial of investigational suvodirsen (WVE-210201) in boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 51 skipping. The company also announced the design of its planned Phase 2/3 clinical trial of suvodirsen in DMD, DYSTANCE 51. The Phase 1 data and DYSTANCE 51 details will be presented today at the 2019 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in Orlando, Florida.

“We are delighted that suvodirsen's Phase 1 results demonstrate a favorable safety and tolerability profile that allow us to proceed rapidly into Phase 2/3 clinical development with doses we expect to be within the therapeutic window. Later this year, we expect to report interim efficacy data from the ongoing open-label extension study of suvodirsen and intend to use those data as an important component of a submission for accelerated approval in the United States,” said Michael Panzara, MD, MPH, Chief Medical Officer of Wave Life Sciences. “We truly appreciate the boys and families that made this trial possible.”

Phase 1 Clinical Trial Results
Wave’s Phase 1 clinical trial was a global, multicenter, double-blind, placebo-controlled study designed to evaluate the safety, tolerability and plasma concentrations of single ascending doses of suvodirsen administered intravenously. Thirty-six patients received a dose of 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 5 mg/kg, 7 mg/kg or 10 mg/kg of suvodirsen (n=26) or placebo (n=10) in five ascending dose cohorts and were followed for 85 days. No serious adverse events, deaths or discontinuations due to adverse events were reported in any study patients treated with suvodirsen.

In December 2018, the company selected an initial dose for the DYSTANCE 51 Phase 2/3 clinical trial based on results from the first four cohorts (0.5 mg/kg – 5 mg/kg) of the Phase 1 clinical trial. Key findings from suvodirsen patients in those four cohorts (n=24) and all placebo patients (n=10) include:

- Suvodirsen was generally safe and well tolerated;
- 67% of patients who received suvodirsen (16/24) and 80% of patients who received placebo (8/10) experienced one or more adverse events;
- The most common adverse events occurring in two or more patients who received suvodirsen were pyrexia, headache, vomiting and tachycardia, consistent with infusion-associated reactions;
- Adverse events in patients receiving suvodirsen were mild to moderate in intensity and resolved spontaneously or with symptomatic treatment;
- No clinically relevant changes were observed in renal or hepatic parameters or platelet levels;
- In patients receiving 5 mg/kg of suvodirsen, the adverse events that occurred within 24 hours of infusion were associated with transient increases in high-sensitivity C-reactive protein and complement factor Bb levels, both of which were resolved within a week; and
- No changes were observed in complement C3 levels.

Based on results of the first four ascending dose cohorts, the independent Safety Monitoring Committee of the Phase 1 clinical trial endorsed continued dose exploration by proceeding to the last planned cohort. Doses of 7 mg/kg or 10 mg/kg of suvodirsen were administered to two patients in the fifth cohort and were associated with similar adverse events as those observed at lower doses but were more severe in intensity. The full data from the Phase 1 clinical trial will be presented in an oral presentation and poster at today’s MDA conference.

“The safety profile of suvodirsen observed in this study is encouraging and supports continued progression to a Phase 2/3 study,” said Kathryn Wagner, MD, PhD, chair of the suvodirsen clinical advisory committee and director of the Center for Genetic Muscle Disorders at the Kennedy Krieger Institute at the Johns Hopkins School of Medicine. “These data, along with Wave’s innovative approach to chemical design and clinical development, make me optimistic about suvodirsen’s potential as a possible DMD treatment.”

Design for Phase 2/3 DYSTANCE 51 Clinical Trial
In a second poster, Wave will present the design of DYSTANCE 51, a global, multicenter, randomized, double-blind, placebo-controlled Phase 2/3 efficacy and safety clinical trial of suvodirsen in DMD patients amenable to exon 51 skipping. This clinical trial is designed to enroll boys who are between 5 and 12 years of age (inclusive) with a genetically confirmed diagnosis of DMD amenable to exon 51 skipping therapy. Patients will be randomized to receive 4.5 mg/kg or 3 mg/kg of suvodirsen or placebo administered intravenously once weekly for 48 weeks. The 4.5 mg/kg dose in DYSTANCE 51 provides approximately the same amount of active ingredient as the 5 mg/kg dose in the Phase 1 clinical trial. Both doses have been selected based on the Phase 1 clinical trial results as well as data from *in vitro* and *in vivo* nonclinical studies.

The DYSTANCE 51 primary efficacy endpoints will measure change in dystrophin protein level and change in the North Star Ambulatory Assessment score. In addition, this Phase 2/3 clinical trial will include multiple functional outcome measures as secondary efficacy endpoints. DYSTANCE 51 is expected to be initiated in July 2019 and the company intends to use the results of this trial to seek regulatory approvals globally.

Earlier this year, Wave announced that the DYSTANCE 51 clinical trial was selected for the U.S. Food and Drug Administration (FDA) pilot program for

complex innovative trial designs. As a participant in the pilot program, the company has additional opportunities to meet with FDA staff to discuss the design elements of the trial, including the potential use of Bayesian methods to adapt the trial with the aim of allowing for more efficient and productive clinical determinations.

Ongoing Open-label Extension Study
Suvodirsen is currently being studied in an ongoing, multi-dose, open-label extension (OLE) study initiated in August 2018 with patients from the Phase 1 clinical trial. The company expects to report 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 serve as an important component of a submission to the FDA for accelerated approval.

Investor Conference Call and Webcast
Wave management will host an investor webcast and conference call today at 7:30 a.m. ET to discuss the Phase 1 safety and tolerability results of suvodirsen, as well the design of the DYSTANCE 51 Phase 2/3 clinical trial. The conference call may be accessed by dialing (866) 220-8068 for participants based in the United States. or +1 (470) 495-9153 for participants based outside the United States and entering conference ID 8975967. The accompanying slide presentation and live webcast may be accessed by visiting the investor relations section of the Wave Life Science corporate website at www.ir.wavelifesciences.com. Following the webcast, a replay will be available on the website.

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.

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. In addition, the planned Phase 2/3 clinical trial of suvodirsen, DYSTANCE 51, was the first study ever selected for the FDA pilot program for complex innovative trial designs (CID).

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 planned presentation today of the final results from the Phase 1 clinical trial of suvodirsen in DMD, the expected timing of initiation of the Phase 2/3 clinical trial for suvodirsen in DMD, the plans to report interim efficacy data from the ongoing open-label extension study with patients from the Phase 1 clinical trial of suvodirsen in DMD, the belief that the safety and tolerability data from the Phase 1 clinical trial supports initiation of a Phase 2/3 clinical trial, Wave's intention to use the results of the Phase 2/3 trial to seek regulatory approvals, Wave's plans and expectations regarding the design of the Phase 2/3 clinical trial, and Wave's expectations regarding the selection of the Phase 2/3 trial for the FDA pilot program for complex innovative trial design. 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. These risks and uncertainties include but are not limited to the following: Wave's current and planned clinical trials, other studies for suvodirsen, and Wave's other product candidates may not be successful or may take longer and be more costly than anticipated; product candidates that appeared promising in earlier research and clinical trials may not demonstrate safety and/or efficacy in later-stage or larger-scale clinical trials; and the other risk factors discussed under the heading "Risk Factors" contained in Wave's Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission (SEC), as well as in other filings Wave makes with the SEC from time to time. All statements contained in this press release are made only as of the date of this press release, and Wave undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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