Preclinical Data Supporting Wave Life Sciences ALS and FTD Programs Presented at 28th International Symposium on ALS/MND

December 11, 2017

Lead candidate targets C9ORF72; in vivo animal data demonstrate potent, sustained and preferential knockdown of toxic biomarkers associated with ALS and FTD

CAMBRIDGE, Mass., Dec. 11, 2017 (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 data from preclinical studies of WVE-3972-01, the company's investigational stereopure antisense oligonucleotide designed to target the pathogenic allele of the *C9ORF72* gene for the treatment of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). In preclinical studies, WVE-3972-01 demonstrated substantial reduction in disease-associated biomarkers and superior potency to stereorandom oligonucleotides. Wave Life Sciences intends to initiate clinical trials of WVE-3972-01 in ALS and FTD in Q4 2018.

Data from *in vitro* and *in vivo* studies of stereorandom and stereopure oligonucleotides, including WVE-3972-01, were presented by Robert Brown, Jr., DPhil, MD at the 28th International Symposium on ALS/MND in Boston during the closing plenary session on December 10, 2017. Dr. Brown is Chair and Professor of Neurology at the University of Massachusetts Medical School.

"The degree of silencing of C9orf72 by WVE-3972-01 and the potency of this stereopure antisense oligonucleotide preclinically are quite compelling," said Dr. Brown. "We are very excited at the prospect of seeing these unique oligonucleotides in clinical trials in C9orf72 patients in the near term."

Mutations in the *C9ORF72* gene are believed to be the most common cause of familial ALS and FTD. These mutations cause the production of repeat-containing transcripts, resulting in accumulation of RNA foci and an increase in dipeptide repeat proteins in the brain and spinal cord. *C9ORF72*-associated diseases such as familial ALS and FTD are postulated to arise from a reduction of normal C9orf72 protein or a gain in toxic RNA foci or dipeptide repeat proteins.

Wave Life Sciences, in collaboration with Dr. Brown and his team, showed that WVE-3972-01 preferentially reduced repeat-containing transcripts versus all transcripts in neurons derived from ALS patients with a *C9ORF72* mutation and demonstrated greater potency when compared with stereorandom oligonucleotides of the same sequence. *In vivo* studies conducted in a transgenic animal model containing the mutated *C9ORF72* gene demonstrated that WVE-3972-01 produced a significant and sustained preferential knockdown of repeat-containing transcripts, RNA foci and dipeptide repeat proteins without altering total C9orf72 protein levels. When measured at eight weeks after treatment, RNA foci in the spinal cord were reduced by 70%. Dipeptide repeat proteins achieved a maximum reduction of 76% and 87% in the spinal cord and the cortex, respectively, and remained significantly low through eight weeks, the last observed time point.

"The high potency and sustained effect seen *in vivo* on important preclinical C9orf72 biomarkers make us optimistic regarding the potential of WVE-3972-01," said Michael Panzara, MD, MPH, Franchise Lead, Neurology at Wave Life Sciences. "The reduction of mutant C9orf72 proteins with preservation of healthy C9orf72 proteins is likewise encouraging. We look forward to working with the ALS and FTD communities to bring WVE-3972-01 into clinical trials in Q4 2018."

In January 2017, Wave Life Sciences and the University of Massachusetts Medical School established a collaboration to further understand neurodegenerative and neuromuscular diseases, including ALS, and characterize the pharmacology of oligonucleotides. Research under this collaboration is conducted by Dr. Brown, an internationally known researcher and physician leading basic and clinical research on ALS and other neurodegenerative diseases.

Today, Wave Life Sciences will be hosting an expert breakfast discussing the company's neurology pipeline, which will include Dr. Brown presenting data from the preclinical studies of WVE-3972-01. A replay of this presentation will be available following the presentation and accessible on the company's website for a limited time.

About Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD)

ALS is a fatal, neurodegenerative disease in which the progressive degeneration of motor neurons in the brain and spinal cord leads to the inability to initiate or control muscle movement. People with ALS may lose the ability to speak, eat, move and breathe. ALS affects as many as 30,000 people in the United States.

FTD is a fatal, neurodegenerative disease in which progressive nerve cell loss in the brain's frontal lobes and temporal lobes leads to personality and behavioral changes, as well as the gradual impairment of language skills. It is the second most common form of early-onset dementia after Alzheimer's disease in people under the age of 65. FTD affects approximately 55,000 people in the United States.

ALS and FTD can be caused by mutations in the *C9ORF72* gene, which provides instructions for making protein found in various tissues, including nerve cells in the cerebral cortex and motor neurons. The *C9ORF72* genetic mutation consists of hundreds to thousands hexanucleotide repeats compared to two to 23 in wild-type transcripts, causing the formation and accumulation of mutant transcripts and proteins in brain tissue. Mutations of the *C9ORF72* gene are present in approximately 40% of familial ALS cases and 8% to 10% of sporadic ALS cases. In FTD, the mutations appear in 38% of familial cases and 6% of sporadic cases.

About Wave Life Sciences

Wave Life Sciences is a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases. Our chemistry platform enables the creation of highly specific, well characterized oligonucleotides designed to deliver superior efficacy and safety across multiple therapeutic modalities. Our pipeline is initially focused on neurological disorders and extends across several other therapeutic areas.

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, statements regarding the data from preclinical studies of our ALS and FTD candidate (WVE-3972-01); the degree to which our preclinical data will translate into clinical results; the anticipated timing of our potential future clinical trials for ALS and FTS; our ability to demonstrate the therapeutic benefits of our ALS and FTD candidate in clinical trials; our understanding of the correlation between the *C9orf72* gene and the cause of ALS and FTD, uncertainties inherent in research and drug development of WVE-3972-01; and Wave's strategy and business plans. 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 Wave 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, uncertainties inherent in research and drug development, risks and uncertainties related to the delay of any current or planned clinical trials or the development of WVE-3972-01, the ability of our preclinical programs to produce data sufficient to support our clinical trial applications and the timing thereof, potential future clinical data and analysis, as well as those discussed or identified in Wave's public filings with the Securities and Exchange Commission (SEC). These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Wave's Annual Report on Form 10-K for the year ended December 31, 2016, as filed with the SEC on March 16, 2017, and in other filings that Wave makes with the SEC from time to time. Any forward-looking statements contained in this press release represent Wave's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Wave explicitly disclaims any obligation to update any forward-looking statements.

Investor Contact:

Jillian Connell
617-949-2981
jconnell@wavelifesci.com

Media Contact:

Jose Juves
617-949-4708
jjuves@wavelifesci.com

Patient Contact:

Wendy Erler
617-949-2898
werler@wavelifesci.com

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