Wave Life Sciences Initiates Two Phase 1b/2a Clinical Trials: PRECISION-HD1 and PRECISION-HD2 in Patients with Huntington's Disease

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Trials Evaluate the First Allele-Specific Investigational Drugs for Huntington's Disease, WVE-120101 and WVE-120102

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 17, 2017-- Wave Life Sciences Ltd. (NASDAQ:WVE), a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases, today announced the initiation of the Company's PRECISION-HD program, which includes PRECISION-HD1 and PRECISION-HD2, the Company's two Phase 1b/2a clinical trials evaluating WVE-120101 and WVE-120102, respectively, for patients with Huntington's disease (HD).

"Wave's PRECISION-HD program is the first to target the underlying cause of Huntington's disease with an allele-specific approach," said Michael Panzara, MD, MPH, Neurology Franchise Lead of Wave Life Sciences. "Obtaining approvals to initiate these global studies as part of our first clinical program marks an important milestone for Wave. More importantly, these investigational compounds have the potential to address a critical unmet need for the HD patient community where no disease-modifying treatments are currently approved."

PRECISION-HD1 and PRECISION-HD2 are Phase 1b/2a multicenter, randomized, double-blind, placebo-controlled studies that will primarily evaluate the safety and tolerability of single and multiple doses of WVE-120101 and WVE-120102, respectively, administered intrathecally in HD patients. Additional exploratory objectives include assessing the impact that each compound has on the toxic mutant protein known to cause loss of brain cells in HD, as well as evaluating potential clinical effects and impact on brain atrophy as measured by magnetic resonance imaging (MRI). Both PRECISION-HD trials will follow the same protocol, and each will target a single nucleotide polymorphism, or "SNP," that marks a separate and distinct location on the mutant *huntingtin* (*HTT*) gene transcript. Wave intends to enroll approximately 50 patients globally in each of the two studies through multiple sites, in Canada initially, with Europe and the United States to follow.

The PRECISION-HD trials for WVE-120101 and WVE-120102 will include adult patients with early manifest HD who carry a SNP at the rs362307 ("SNP1") or the rs362331 ("SNP2") location, respectively. Potential HD patients for the PRECISION-HD program will be pre-screened for the presence of SNP1 or SNP2, and directed to the appropriate study upon qualifying for entry. Approximately two-thirds of all HD patients are expected to carry either SNP1, SNP2, or both, in association with the HD gene.

SNPs are a common type of genetic variation that normally occur in all humans, but may also act as biological markers to aid in locating genes associated with a particular disease. Previous HD research has identified multiple SNPs that are associated with the disease-causing expanded cytosine-adenine-guanine (CAG) repeat, which is an abnormality present in all HD patients that results in the production of mutant huntingtin protein, and causes HD. Therefore, Wave is utilizing common SNPs to precisely target the underlying cause of the disease.

"Reducing the disease-causing mutant huntingtin while preserving the healthy protein would be an important breakthrough for the HD community," said Dr. Edward Wild, Principal Researcher at University College London Huntington's Disease Centre, Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, London, and member of the PRECISION-HD Clinical Advisory Committee. "The pre-clinical data for Wave's targeted compounds are encouraging and I am thrilled that we are beginning to explore the potential of these compounds in HD patients in this exciting programme."

About Huntington's Disease (HD)

HD is a debilitating and ultimately fatal autosomal dominant disorder, characterized by cognitive decline, psychiatric illness and chorea. HD causes nerve cells in the brain to deteriorate over time, affecting thinking ability, emotions and movement. HD is caused by an expanded cytosine-adenine-guanine (CAG) triplet repeat in the *huntingtin* (*HTT*) gene that results in production of mutant HTT (mHTT) protein. Accumulation of mHTT causes progressive loss of neurons in the brain. Wild-type, or healthy, HTT protein is critical for neuronal function, and suppression may have detrimental long-term consequences. Approximately 30,000 people in the United States have symptomatic HD and more than 200,000 others are at risk for inheriting the disease. There are currently no approved disease-modifying therapies available.

About WVE-120101 and WVE-120102

WVE-120101 and WVE-120102 are investigational stereopure antisense oligonucleotides designed to selectively target the m*HTT* mRNA transcript of SNP rs362307 (SNP1) and SNP rs362331 (SNP2), respectively. These are the two most common SNPs associated with the mutant allele, which is believed to encompass approximately two-thirds of the HD patient population. *In vitro* studies in patient-derived cell lines have shown that WVE-120101 and WVE-120102 selectively reduce levels of m*HTT* mRNA and protein, while leaving wt*HTT* mRNA and protein largely intact.

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 Information

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 initiation of clinical trials for WVE-120101 and WVE-120102, including Wave's ability to screen and enroll patients; Wave's ability to implement its global clinical development plans for WVE-120101 and WVE-120102 for the treatment of Huntington's disease; the potential benefits of Wave's allele-specific approach; 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, future clinical data and analysis, the decisions of global regulatory authorities as to whether and when to approve any application that may be filed for any of our candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, our ability to benefit from external growth opportunities and/or obtain regulatory clearances, risks associated with intellectual property, volatile economic conditions, healthcare reform, as well as those discussed or identified in Wave's public filings with the 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 Securities and Exchange Commission (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.

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Media and Investors
WAVE Life Sciences
Jillian Connell, 617-949-2981
jconnell@wavelifesci.com