Wave Life Sciences and Takeda Form Global Strategic Collaboration to Advance Therapies for Central Nervous System Disorders

February 20, 2018

Wave to receive at least $230 million, including $110 million in upfront cash, $60 million in equity investment and at least $60 million in research support

Takeda to receive option to co-develop and co-commercialize investigational therapies in HD, ALS, FTD and SCA3 under a global 50:50 profit-split

Takeda to receive right to license additional preclinical CNS programs; Wave eligible to receive more than $1 billion in potential precommercial milestones

CAMBRIDGE, Mass., Feb. 20, 2018 (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 the formation of a global strategic collaboration with Takeda Pharmaceutical Company Limited to discover, develop and commercialize nucleic acid therapies for disorders of the central nervous system (CNS). Under the collaboration, Wave will provide Takeda the option to co-develop and co-commercialize programs in Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) and spinocerebellar ataxia type 3 (SCA3). In addition, Takeda will have the right to license multiple preclinical programs targeting CNS disorders, including Alzheimer's disease and Parkinson's disease. Wave will continue to independently advance its activities in neuromuscular diseases, including its lead clinical program for the treatment of Duchenne muscular dystrophy (DMD).

Under terms of the two-component agreement, Takeda will make an initial payment of $110 million to Wave and purchase $60 million of Wave's ordinary shares at $54.70 per share. Takeda will also fund at least $60 million of Wave research over a four-year period to advance multiple preclinical targets selected by and licensed to Takeda.

"We are thrilled to be joining with Takeda in this ambitious alliance to bring meaningful therapies to patients suffering from devastating neurological diseases," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "This partnership provides additional resources to advance our clinical programs through multiple data readouts while continuing to expand our pipeline in neurology and other therapeutic areas. We look forward to working with Takeda and leveraging our expertise in oligonucleotides and clinical capabilities to grow our company and continue to make scientific and medical advances on behalf of patients."

"At Takeda, we are focused on partnering with companies that share our research focus and commitment to deliver transformative medicines to patients," Daniel Curran, MD, Head, Center for External Innovation at Takeda. "Wave's expertise in optimizing oligonucleotides offers a complementary approach to programs that Takeda is currently pursuing for neurological disorders, maximizing our potential for success, and their pipeline and focus are closely aligned with our own."

The first component of the agreement grants Takeda with the option to co-develop and co-commercialize the following nucleic acid investigational therapies upon Wave demonstrating proof of mechanism in initial clinical studies:

- WVE-120101 and WVE-120102, which selectively target the mutant allele of the *huntingtin (HTT)* gene and are currently in Phase 1b/2a clinical trials for the treatment of HD
- WVE-3972-01, which targets the *C9ORF72* gene and is expected to be evaluated in clinical studies for the treatment of ALS and FTD beginning in Q4 2018
- Program targeting the *ATXN3* gene for the treatment of SCA3

Upon opt-in by Takeda on any individual program, Wave will receive an opt-in payment and will lead manufacturing and joint clinical co-development activities; Takeda will lead joint co-commercial activities in the United States and all commercial activities outside of the United States. Global costs and potential profits will be shared 50:50 and Wave will be eligible to receive development and commercial milestone payments.

The second component of the strategic collaboration provides Takeda with the right to license multiple preclinical programs for CNS indications, including Alzheimer's disease and Parkinson's disease. During a four-year term, the companies may collaborate on up to six preclinical targets at any one time. Takeda will fund at least $60 million of Wave's preclinical activities and reimburse Wave for agreed-upon additional expenses. Assuming Takeda advances six programs that achieve regulatory approval and commercial milestones, Wave will be eligible to receive more than $2 billion in cash milestone payments, of which more than $1 billion would be in precommercial milestone payments. Wave is also eligible to receive tiered high single-digit to mid-teen royalty payments on global commercial sales of each licensed program.

The collaboration agreement will become effective upon satisfaction of customary closing conditions, including the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976.

Outside of the collaboration with Takeda, Wave continues to independently advance its activities in neuromuscular diseases, including its lead DMD program, an investigational therapy targeting exon 51 (WVE-210201) currently in a Phase 1 clinical trial. Wave's next DMD program, targeting exon 53, is expected to initiate clinical development in Q1 2019. The company also continues to expand its preclinical research pipeline in other therapeutic areas, including metabolic liver diseases in collaboration with Pfizer and ophthalmology where Wave has wholly-owned discovery programs.

About WVE-120101 and WVE-120102

HD is an autosomal-dominant, progressive neurodegenerative disorder caused by an expanded cytosine-adenine-guanine (CAG) triplet repeat in the *HTT* gene that results in production of mutant HTT (mHTT) protein. Accumulation of mHTT protein causes progressive loss of neurons in the brain. Wild-type, or healthy, HTT (wtHTT) protein is critical for neuronal function, and research suggests that long-term suppression may have detrimental consequences. 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. *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 WVE-3972-01

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. WVE-3972-01 is an investigational stereopure antisense oligonucleotide designed to preferentially target the pathogenic allele of the *C9ORF72* gene. *In vivo* studies conducted in a transgenic animal model containing the mutated *C9ORF72* gene demonstrated that WVE-3972-01 produced significant and sustained preferential knockdown of disease-associated biomarkers such as repeat-containing transcripts, RNA foci and dipeptide repeat proteins without altering total C9ORF72 protein levels.

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. For more information, please visit www.wavelifesci.com.

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 collaboration and license agreement between Wave and Takeda, including anticipated payments, as well as the future discovery, development, manufacture and commercialization of potential therapies for CNS disorders under the agreement; Wave's and Takeda's ability to successfully develop and commercialize potential therapies for CNS disorders; 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 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, risks and uncertainties related to Wave's ability to successfully advance multiple potential preclinical programs simultaneously on its platform; the delay of any current or planned clinical trials or the other development activities for Wave's investigational therapies; Wave's ability to successfully demonstrate the safety and efficacy of its investigational therapies; the preclinical and clinical results of Wave's investigational therapies; actions of regulatory authorities that may affect the initiation, timing and progress of clinical trials; and Wave's ability to successfully commercialize any investigational therapies that receive regulatory approval. 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 other filings that Wave may make 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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Source: Wave Life Sciences