Wave Life Sciences Announces Approval of First Clinical Trial Application for RestorAATion-2 Trial of WVE-006 in Individuals with Alpha-1 Antitrypsin Deficiency (AATD)

April 30, 2024

Proof-of-mechanism data for WVE-006 in individuals with AATD remain on track for 2024

CAMBRIDGE, Mass., April 30, 2024 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health, today announced the approval of its first clinical trial application (CTA) for its RestorAATion-2 clinical trial of WVE-006, the company's first-in-class RNA editing oligonucleotide, which is being developed for the treatment of alpha-1 antitrypsin deficiency (AATD). WVE-006 is GalNAc-conjugated and subcutaneously administered; it does not use a lipid nanoparticle (LNP) delivery system.

"The approval of our first CTA for the RestorAATion-2 clinical trial of WVE-006 marks an important milestone as we continue extending our leadership in RNA editing. It is also important for the alpha-1 community as WVE-006 has the potential to enable correction of the disease-causing RNA mutation and provide a single therapeutic option regardless of whether patients have AATD liver disease, lung disease or both," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Our rapid progress in dose escalating healthy volunteers enabled us to demonstrate the translation of safety and pharmacokinetics of WVE-006 in humans and quickly identify a starting dose level that, based on preclinical data, is expected to engage the target in patients. With proof-of-mechanism data from RestorAATion-2 expected later this year, we look forward to the opportunity to provide clinical demonstration of RNA editing and proof-of-concept for our wholly owned pipeline of RNA editing candidates."

RestorAATion-2 is a Phase 1b/2a open label study designed to evaluate the safety, tolerability, pharmacodynamics (PD) and pharmacokinetics (PK) of WVE-006 in individuals with AATD who have the homozygous Pi*ZZ mutation. The trial includes both single ascending dose (SAD) and multiple ascending dose (MAD) portions. The company remains on track to deliver proof-of-mechanism data, as measured by restoration of M-AAT protein in serum, in 2024.

GSK has the exclusive global license for WVE-006. Development and commercialization responsibilities will transfer to GSK after Wave completes the RestorAATion-2 study.

In addition to WVE-006, Wave continues to advance its wholly owned RNA editing pipeline across a range of high-impact GalNAc-hepatic and extra-hepatic targets. The company's discovery and development efforts in RNA editing are powered by its proprietary "edit-verse," which leverages genetic datasets and deep learning models to identify new RNA editing targets and edit sites. These targets leverage easily accessible biomarkers, offer efficient paths to proof-of-concept in humans, and represent meaningful commercial opportunities.

About WVE-006
WVE-006 is a first-in-class, GalNAc-conjugated and subcutaneously administered RNA editing oligonucleotide designed to correct the single base mutation in messenger RNA (mRNA) coded by the SERPINA1 Z allele, thereby enabling restoration and circulation of functional M-AAT protein. In preclinical studies, WVE-006 demonstrated potent and durable editing of SERPINA1 Z transcript in mice, restoration of AAT protein up to 30 micromolar, and improvement in several markers of liver disease. WVE-006 is also highly specific with no evidence of bystander editing. Together, these data demonstrate the potential of WVE-006 to address AATD-related liver disease, lung disease, or both.

About Wave Life Sciences
Wave Life Sciences (Nasdaq: WVE) is a biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health. Wave's RNA medicines platform, PRISM ^{TM}, combines multiple modalities, chemistry innovation and deep insights in human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Its toolkit of RNA-targeting modalities includes editing, splicing, RNA interference and antisense silencing, providing Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's diversified pipeline includes clinical programs in Duchenne muscular dystrophy, Alpha-1 antitrypsin deficiency and Huntington's disease, as well as a preclinical program in obesity. Driven by the calling to "Reimagine Possible", Wave is leading the charge toward a world in which human potential is no longer hindered by the burden of disease. Wave is headquartered in Cambridge, MA. For more information on Wave's science, pipeline and people, please visit www.wavelifesciences.com and follow Wave on X (formerly Twitter) and LinkedIn.

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 of WVE-006 to treat AATD; our expectations and anticipated timing for delivering proof-of-mechanism clinical data in AATD patients treated with WVE-006; and our understanding that WVE-006 is the most advanced candidate for AATD designed to restore functional wild-type AAT protein and reduce Z-AAT protein aggregation. 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 and actual results may differ materially from those indicated by these forward-looking statements as a result of these risks, uncertainties and important factors, 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 circumstance.

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Source: Wave Life Sciences USA, Inc.