Wave Life Sciences Announces Submission of First Clinical Trial Application for WVE-006, the First-ever RNA Editing Clinical Candidate, and Plans for Upcoming Virtual "R&D Day"

September 5, 2023

WVE-006 is the first-ever RNA editing program to enter clinical development and is designed to restore production and circulation of functional, wild-type alpha-1 antitrypsin (AAT) protein and reduce levels of mutant Z-AAT protein, thereby addressing alpha-1 antitrypsin deficiency-related lung disease, liver disease or both

Wave expects to initiate dosing in the first-in-human clinical program in 4Q 2023 and deliver AAT protein restoration data from AATD patients treated with WVE-006 in 2024

Under its collaboration with GSK, Wave is eligible to receive substantial milestone payments for WVE-006 in 2023 and beyond

Wave plans to host a virtual "R&D Day" on September 28, 2023; topics to include the WVE-006 clinical program and how Wave is extending its leadership in RNA editing with additional programs

CAMBRIDGE, Mass., Sept. 05, 2023 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced the submission of its first clinical trial application (CTA) for WVE-006 in alpha-1 antitrypsin deficiency (AATD). WVE-006 is a first-in-class, GalNAc-conjugated RNA editing oligonucleotide ("AIMer") and is designed to correct the single base mutation in messenger RNA (mRNA) coded by the *SERPINA1* Z allele, thereby enabling restoration and circulation of functional, wild-type alpha-1 antitrypsin (M-AAT) protein. The WVE-006 clinical program will be highlighted in Wave's virtual "R&D Day" on September 28, 2023 at 10:00 a.m. ET, among other programs.

"With the submission of the first CTA for WVE-006, we have officially initiated clinical development of the industry's first-ever RNA editing therapeutic candidate," said Anne Marie Li-Kwai-Cheung, Chief Development Officer at Wave Life Sciences. "We designed WVE-006 to correct the most common underlying genetic mutation that causes AATD, providing an innovative therapeutic option for individuals with lung disease, liver disease or both. Indeed, our preclinical data support this profile, with mouse models showing restored AAT protein well above 11 micromolar, as well as improvement in several markers of liver disease and inhibition of neutrophil elastase. As a GalNAc-RNA editing oligonucleotide, WVE-006 is reversible and re-dosable, with potential for infrequent subcutaneous dosing. WVE-006 is highly specific with no evidence of bystander editing and, by virtue of the mechanism of action, no permanent changes to the genome that occur with DNA-targeting approaches. For these reasons, we believe WVE-006 has potential to revolutionize how AATD is treated."

The current clinical development plan for WVE-006 includes healthy volunteers as well as individuals with AATD who have the homozygous PiZZ mutation, and is designed to provide an efficient path to proof-of-mechanism as measured by restoration of M-AAT protein in serum. Wave expects to initiate dosing in healthy volunteers in the fourth quarter of 2023 and deliver proof-of-mechanism data in individuals with AATD in 2024.

"WVE-006 is on a path to potentially deliver the first-ever proof-of-mechanism clinical data for an RNA editing therapeutic. Positive data would be a pivotal milestone for people living with AATD and would unlock the potential of RNA editing more broadly. Additionally, WVE-006 is a foundational component of our collaboration with GSK and carries with it meaningful milestone and royalty payments, including near-term clinical milestones," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "RNA editing is a promising new therapeutic modality, capable of accessing untapped areas of disease biology. We are incredibly proud to be pioneers leading the way forward in RNA editing, and we plan to share more updates on AATD and other RNA editing programs during our R&D Day later this month."

Earlier this year, Wave commenced its strategic collaboration with GSK to advance transformative RNA medicines using Wave's multimodal RNA platform, including WVE-006. Wave received $170 million in upfront cash and equity and is also receiving research funding. Wave is eligible for up to $3.3 billion in potential milestone payments, including near-term preclinical and clinical milestones, as well as royalties, for WVE-006 and GSK's eight collaboration programs. For WVE-006, Wave is eligible to receive up to $225 million in development and launch milestone payments, and up to $300 million in sales-related milestone payments, as well as double-digit tiered royalties as a percentage of net sales up to the high teens.

Wave expects that its cash and cash equivalents will be sufficient to fund operations into 2025. Wave does not include future milestones or other contingent payments in its cash runway.

Wave Virtual R&D Day
A link to register for the event is available here. A live webcast of the event can be accessed by visiting "Investor Events" on the investor relations section of the Wave Life Sciences website: https://ir.wavelifesciences.com/events-and-presentations. Following the live event, an archived version of the webcast will be available on the Wave Life Sciences website.

About WVE-006 and AATD
WVE-006 is a clinical-stage GalNAc-conjugated investigational RNA editing oligonucleotide for the treatment of alpha-1 antitrypsin deficiency (AATD). AATD is an inherited genetic disorder that is commonly caused by a G-to-A point mutation ("Z allele") in the *SERPINA1* gene. This mutation leads to lung disease due to a lack of wild-type alpha-1 antitrypsin (M-AAT) function in lungs, and it leads to liver disease due to aggregation of misfolded Z-AAT protein in hepatocytes. There are approximately 200,000 patients in the United States and Europe who have Z mutations on both alleles, known as the PiZZ genotype. Augmentation therapy via delivery of AAT protein is currently the only treatment option for AATD lung disease and requires weekly intravenous infusions. There are currently no treatments for AATD liver disease, other than liver transplantation.

About AIMers
A-to-I(G) RNA editing oligonucleotides ("AIMers") are designed to edit specific sites on an RNA transcript, thereby avoiding permanent changes to the genome that occur with DNA-targeting approaches. Rather than using an exogenous editing enzyme, AIMers recruit proteins that exist in the body, called ADAR enzymes, which naturally edit certain adenine (A) bases to inosine (I). Because I is read as G (guanine) by the cellular translational machinery, sequence-directed editing with ADAR has the potential to revert transcripts with single G-to-A point mutations that cause genetic diseases. This approach redirects a natural system for therapeutic purposes, enables simplified delivery without viral particles or liposomes, and avoids the risk of irreversible off-target effects of DNA-targeting approaches. AIMers are short in length, fully chemically modified, and use novel chemistry, including proprietary PN backbone modifications and chiral control, that make them distinct from other ADAR-mediated editing approaches.

About Wave Life Sciences
Wave Life Sciences (Nasdaq: WVE) is a clinical-stage RNA 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, our expectations for our GalNAc-conjugated RNA editing oligonucleotides (AIMers), including WVE-006, and the anticipated therapeutic benefits thereof, including the potential of WVE-006 to treat AATD; the anticipated timing to initiate dosing in the first-in-human clinical program with WVE-006, and the associated delivery of AAT protein restoration data from AATD patients treated with WVE-006; the future performance and results of our clinical programs; our expectations for delivering proof-of-mechanism clinical data for an RNA editing therapeutic; 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; our expectations regarding the ability of our AIMers to address diseases of many different tissues and cell types; the potential benefits of our AIMers compared with other RNA base editing approaches; and the potential achievement of milestones under our collaborations and receipt of cash payments therefor. 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 circumstances.

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