Wave Life Sciences and GSK Announce Collaboration to Drive Discovery and Development of Oligonucleotide Therapeutics Focusing on Novel Genetic Targets

December 13, 2022

Wave receives upfront payment of $170 million in cash and equity, also eligible to receive milestone payments and royalties

Collaboration brings together Wave's PRISM™ oligonucleotide platform and GSK's expertise in genetics and genomics

GSK to advance up to eight preclinical programs

Additionally, GSK receives exclusive global license to Wave's preclinical, potential first-in-class RNA editing program, WVE-006, to treat alpha-1 antitrypsin deficiency, a disease that impacts the lungs and liver

Wave to advance up to three preclinical programs for targets informed by GSK's novel insights

Wave to host investor conference call and webcast at 8:30 a.m. ET today

CAMBRIDGE, Mass. and LONDON, Dec. 13, 2022 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases, and GSK plc (LSE/NYSE: GSK) today announced a strategic collaboration to advance oligonucleotide therapeutics, including Wave's preclinical RNA editing program targeting alpha-1 antitrypsin deficiency (AATD), WVE-006. The discovery collaboration has an initial four-year research term. It combines GSK's unique insights from human genetics, as well as its global development and commercial capabilities, with Wave's proprietary discovery and drug development platform, PRISM™.

Oligonucleotides are short strands of DNA or RNA that can reduce, restore, or modulate RNA through several different mechanisms. The unique capability of oligonucleotides to address a wide range of genomic targets in multiple therapeutic areas is enabling new opportunities to treat a range of human diseases, including diseases where no medicines currently exist or that have historically been difficult to treat with small molecules or biologics.

Wave's PRISM platform is the only oligonucleotide platform offering three RNA-targeting modalities (editing, splicing, and silencing, including siRNA and antisense). Importantly, these modalities incorporate novel chemistry, including PN backbone chemistry and control of stereochemistry, to optimize the pharmacological properties of therapeutic oligonucleotides.

The collaboration includes two main components. The first is a discovery collaboration which enables GSK to advance up to eight programs and Wave to advance up to three programs, leveraging Wave's PRISM platform and GSK's expertise in genetics and genomics. In addition to these programs, GSK receives the exclusive global license for Wave's preclinical program for AATD called WVE-006, which uses Wave's proprietary "AIMer" technology (A-to-I(G) RNA editing). AATD is an inherited genetic disease that affects both the lungs and liver with limited treatment options. Wave's WVE-006 is a first-in-class RNA editing therapeutic that is designed to address both liver and lung manifestations of the disease.

Paul Bolno, MD, MBA, President and Chief Executive Officer, Wave Life Sciences, said: "For the past decade, Wave has been building a unique oligonucleotide platform that combines novel chemistry with the means to optimally address disease biology through multiple therapeutic modalities. In 2022, we started to deliver on the promise of our platform with the first data showing translation in the clinic for our next-generation stereopure PN-chemistry containing candidates. Now with our GSK collaboration, we are excited to leverage their expertise in genetics to continue building a differentiated oligonucleotide pipeline, with a focus on our best-in-class RNA editing and upregulation capability. Additionally, GSK is the ideal partner for our WVE-006 program, due to their longstanding history and global reach in respiratory diseases. The collaboration meaningfully extends our cash runway into 2025 and offers the potential for significant future milestones, providing new resources to deliver life-changing medicines to patients."

Tony Wood, President and Chief Scientific Officer, GSK, said: "Oligonucleotide therapeutics are becoming a mainstream modality, and this collaboration will enable us to use our leading position in human genetics and genomics to advance novel oligonucleotide therapies. Pairing GSK's genetic expertise with the best-in-class PRISM™ platform enables us to accelerate drug discovery for newly-identified targets, by matching target to modality. The addition of WVE-006 complements more advanced, clinical-phase oligonucleotides in our pipeline, including bepirovirsen for chronic hepatitis B and GSK4532990 for non-alcoholic steatohepatitis (NASH)."

Bepirovirsen, an investigational antisense oligonucleotide for the potential treatment of chronic hepatitis B infection, is now entering Phase III trials, and GSK4532990, a siRNA oligonucleotide, is progressing to Phase II for NASH. WVE-006 brings a third oligonucleotide into GSK's portfolio that has the potential to be a first-in-class AATD treatment for both lung and liver disease and is a well-understood genetic target, contributing to GSK's pipeline that is now more than 70% genetically validated.

The companies expect to pursue targets across multiple disease areas, given preclinical data indicating Wave oligonucleotides can distribute to various tissues and cells without complex delivery vehicles.

Terms of the Collaboration
Under the terms of the agreement, Wave will receive an upfront payment of $170 million, which includes a cash payment of $120 million and a $50 million equity investment.

For the WVE-006 program, 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 tiered sales royalties. Development and commercialization responsibilities will transfer to GSK after Wave completes the first-in-patient study.

For each of GSK's eight collaboration programs, Wave will be eligible to receive up to $130-$175 million in development and launch milestones and $200 million in sales-related milestones, along with tiered sales royalties. Wave will lead all preclinical research for GSK and Wave programs up to investigational new drug (IND) enabling studies. GSK collaboration programs will transfer to GSK for IND-enabling studies, clinical development, and commercialization. The collaboration includes an option to extend the research term for up to three additional years, expanding the number of programs available to both parties.

The equity investment and collaboration agreement will complete at the same time and are conditional upon customary conditions including regulatory review by the appropriate regulatory agencies under the Hart-Scott-Rodino Act.

Investor Conference Call and Webcast
Wave management will host an investor conference call today at 8:30 a.m. ET to discuss the strategic collaboration announcement. The webcast of the conference call and corresponding slide presentation may be accessed by visiting "Events" on the investor relations section of the Wave Life Sciences corporate website: ir.wavelifesciences.com/events-and-presentations.

Analysts planning to participate during the Q&A portion of the live call can join the conference call at the audio conferencing link available here. Once registered, participants will receive the dial-in information. Following the live event, an archived version of the webcast will be available on the Wave Life Sciences website.

About Oligonucleotides
Oligonucleotide mechanisms that can reduce, increase or modify RNA include silencing (oligonucleotides that promote degradation of the target RNA, including antisense and siRNA); splicing (oligonucleotides that involve binding to the target RNA and modulating its function by promoting exon skipping); and ADAR-mediated RNA editing (oligonucleotides that edit adenosines in target RNAs to correct RNA or modulate protein function or production). GSK's investments in genetics have revealed that a significant number of genetic associations point to proteins where modulation of RNA function and/or expression would likely be the most effective mechanism for therapeutic intervention versus more traditional small molecules and biologic-based therapeutics. Oligonucleotide therapeutics represent a modality that addresses this gap by regulating target expression rather than function.

About AIMers
Wave's AIMers are designed to correct mutations in 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 normal 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 Alpha-1 Antitrypsin Deficiency
Alpha-1 antitrypsin deficiency (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 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 the only treatment option for AATD lung disease and requires weekly intravenous infusions. There are no treatments for AATD liver disease, other than liver transplantation.

About WVE-006
WVE-006 is a PN chemistry-modified GalNAc-conjugated investigational development candidate for the treatment of alpha-1 antitrypsin deficiency (AATD), designed to correct the mutant SERPINA1 Z allele transcript to address both liver and lung manifestations of disease. WVE-006 is a potential first-in-class RNA editing candidate (AIMer) and the most advanced program currently in development using an oligonucleotide to harness an endogenous enzyme for editing. Wave expects to submit clinical trial applications for WVE-006 in 2023.

About Wave Life Sciences
Wave Life Sciences (Nasdaq: WVE) is a clinical-stage genetic 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, statements regarding the collaboration and license agreement between Wave and GSK, including anticipated payments, as well as the discovery, development, manufacture and commercialization of potential oligonucleotide therapeutics under the agreement, 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 programs simultaneously; the delay of any current or planned clinical trials or the other development activities for WVE-006; the effectiveness of PRISM, including our novel PN backbone chemistry modifications; the effectiveness of our novel ADAR-mediated RNA editing platform capability and our AIMers; our dependence on third parties, including contract research organizations, contract manufacturing organizations, collaborators and partners; our ability to obtain, maintain and protect our intellectual property; competition from others developing therapies for similar indications; and the severity and duration of the COVID-19 pandemic and variants thereof, and its negative impact on the conduct of, and the timing of enrollment, completion and reporting with respect to our clinical trials. 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, 2021, as filed with the Securities and Exchange Commission (SEC) on March 3, 2022, 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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