GSK and Wave Life Sciences announce collaboration to drive discovery and development of oligonucleotide therapeutics focusing on novel genetic targets

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For media and investors only

- Collaboration brings together Wave's PRISMTM oligonucleotide platform and GSK's expertise in genetics and genomics

- GSK to advance up to eight preclinical programmes

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

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

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

GSK plc (LSE/NYSE: GSK) and Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced a strategic collaboration to advance oligonucleotide therapeutics, including Wave's preclinical RNA editing programme 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, PRISMTM.

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 optimise 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 programmes and Wave to advance up to three programmes, leveraging Wave's PRISM platform and GSK's expertise in genetics and genomics. In addition to these programmes, GSK receives the exclusive global license for Wave's preclinical programme 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.

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 PRISMTM 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.

Paul Bolno, MD, MBA, President and CEO of 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 programme, 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.

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 programme, 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 commercialisation responsibilities will transfer to GSK after Wave completes the first-in-patient study.

For each of GSK's eight collaboration programmes, 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 programmes up to investigational new drug (IND) enabling studies. GSK collaboration programmes will transfer to GSK for IND-enabling studies, clinical development, and commercialisation. The collaboration includes an option to extend the research term for up to three additional years, expanding the number of programmes 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.

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.

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.

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.

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.

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more

at gsk.com/company

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