Wave Life Sciences Highlights Recent Achievements and Upcoming 2024 Milestones

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Multiple data catalysts across all clinical programs expected throughout 2024, including data for WVE-006 in AATD which would provide first-ever RNA editing proof-of-mechanism in humans

Selection of clinical candidate for GalNAc-siRNA INHBE program in obesity now planned for 3Q 2024, ahead of prior expectation; designed to reduce fat, spare muscle mass, and restore and maintain a healthy metabolic profile

Dosing underway in potentially registrational FORWARD-53 trial evaluating WVE-N531 in DMD; 24-week data, including dystrophin from muscle biopsies, expected in 3Q 2024

WVE-003 30 mg Q8W multi-dose data with extended follow-up on track for 2Q 2024; most advanced program designed to lower mutant HTT while also sparing wild-type HTT

Well-capitalized following $142 million of cash inflows in 4Q 2023, including $115 million from December financing and $27 million in collaboration milestone payments; poised to deliver and advance innovative and sustainable pipeline and unlock significant value

CAMBRIDGE, Mass., Jan. 08, 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 key 2024 milestones across its clinical programs, growing pipeline, and leading RNA medicines platform.

"Wave is uniquely positioned to build the world's leading RNA medicines company, with a clinically validated platform, diversified pipeline aimed at high-impact diseases, and meaningful commercial opportunities. Powered by multiple RNA modalities, a decade of chemistry innovation, and deep genetic insights, we are opening up new areas of disease biology and designing optimal ways of treating rare and common diseases. We expect 2024 will be an inflection year that will drive significant value for Wave, our shareholders, and most importantly, for the patients who will benefit from our research," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences.

Dr. Bolno continued: "This year, we expect the first-ever clinical proof-of-mechanism data for RNA editing with WVE-006 in AATD, which will accelerate additional Wave RNA editing programs. We are rapidly advancing our wholly owned INHBE program for obesity, which is designed to enable healthy, sustainable fat loss and address limitations of GLP1s. We also expect to deliver data demonstrating production of endogenous dystrophin protein in DMD with WVE-N531, as well as multidose data for WVE-003, our HD candidate that is uniquely designed to lower mutant huntingtin and maintain healthy, wild-type huntingtin. These programs underscore our drive to 'Reimagine Possible' for science, for medicine, and for human health."

2024 Priorities and Anticipated Milestones

Advance AATD program to clinical proof-of-mechanism data and unlock additional opportunities for Wave's leading RNA editing capability

WVE-006 in Alpha-1 Antitrypsin Deficiency (AATD) & RNA Editing

- WVE-006 is a GalNAc-conjugated, subcutaneously administered RNA editing oligonucleotide and is the first-ever RNA editing candidate to be evaluated in humans. WVE-006 is uniquely designed to correct the disease-causing SERPINA1 Z transcript mutation in AATD, thereby restoring circulation of wild-type M-AAT protein and reducing Z-AAT protein levels to address both lung and liver manifestations of the disease.
- 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.
- In December 2023, Wave initiated dosing in healthy volunteers in the RestorAATion clinical trial program investigating WVE-006 as a potential treatment for AATD. RestorAATion includes healthy volunteers (RestorAATion-1) as well as individuals with AATD who have the homozygous PiZZ mutation (RestorAATion-2) and is designed to provide an efficient path to proof-of-mechanism as measured by restoration of M-AAT protein in serum.
- GSK has an exclusive global license to WVE-006 as part of its strategic collaboration with Wave. With initiation of dosing in RestorAATion, Wave achieved its first WVE-006 milestone under the collaboration, resulting in a $20 million payment from GSK. Wave is eligible to receive up to $505 million in additional development, launch, and commercial milestone payments, as well as tiered royalties on net sales, from GSK for WVE-006. Development and commercialization responsibilities will transfer to GSK after Wave completes the RestorAATion-2 study.
- Beyond WVE-006, Wave is advancing a pipeline of wholly owned RNA editing therapeutics across a range of high-impact GalNAc-hepatic and extra-hepatic targets.
- **Expected milestones**: Wave plans to deliver proof-of-mechanism data in individuals with AATD in 2024.

Advance INHBE program – first Wave wholly owned program to emerge from GSK collaboration – as well as progress GSK discovery programs under strategic collaboration

INHBE Program in Obesity

- Wave is advancing a novel approach for treating obesity with its GalNAc-small interfering RNA (siRNA) targeting INHBE, which is designed to induce fat loss while preserving muscle mass to restore and maintain metabolic health.
- This program is designed to silence the INHBE gene through RNA knockdown, thereby recapitulating the cardiometabolic

profile of INHBE loss of function (LoF) heterozygous human carriers. These individuals exhibit reduced waist-to-hip ratio and reduced odds of type 2 diabetes and coronary artery disease. INHBE reduction of 50% or greater is expected to restore and maintain a healthy metabolic profile, while preserving muscle mass.
- In September 2023, Wave demonstrated the first *in vivo* proof-of-concept for INHBE silencing, with INHBE mRNA reduction in diet-induced obese mice well beyond the 50% therapeutic threshold, leading to substantially lower body weight and reduction of visceral fat as compared to control.
- **Expected milestones:** Wave has identified potent and highly specific INHBE siRNA leads and now expects to select an INHBE clinical candidate in the third quarter of 2024, ahead of expectation. This would enable clinical trial application (CTA) submission in 2025.

GSK Discovery Collaboration

- Wave continues to advance its discovery collaboration with GSK, which enables GSK to advance up to eight programs and Wave to advance up to three programs (inclusive of INHBE) leveraging Wave's multimodal RNA medicines platform and GSK's expertise in genetics and genomics.
- Wave is eligible for up to $3.3 billion in potential milestone payments for GSK's eight collaboration programs and WVE-006, as well as royalties on net sales.
- **Expected milestones:** Advance collaboration activities with GSK, with potential for additional cash inflows in 2024.

Advance wholly owned DMD program with best-in-class exon skipping to potentially registrational dystrophin data

WVE-N531 in Duchenne Muscular Dystrophy (DMD)

- Wave's WVE-N531 program for boys with DMD amenable to exon 53 skipping is designed to induce production of endogenous, functional dystrophin protein.
- Previous clinical data from the Phase 1b/2a Part A proof-of-concept trial of WVE-N531 in DMD demonstrated high muscle concentrations of WVE-N531 (mean of 42 micrograms/gram) and the highest level of exon skipping ever seen in the clinic (mean exon skipping of 53%; range: 48-62%) after three doses of 10 mg/kg every other week. WVE-N531 appeared safe and well-tolerated, with all treatment-related adverse events being mild.
- In December 2023, Wave announced the initiation of dosing in the potentially registrational Phase 2 FORWARD-53 study and also that the study was fully enrolled.
- **Expected milestones:** Wave expects to deliver data, including dystrophin protein expression from muscle biopsies at 24 weeks, in the third quarter of 2024.

Advance first-in-class, wild-type huntingtin-sparing HD program and deliver multi-dose data set for decision-making

WVE-003 in Huntington's Disease (HD)

- WVE-003 is the most advanced investigational allele-selective HD therapeutic designed to reduce mutant huntingtin (mHTT) protein while also sparing healthy, wild-type huntingtin (wtHTT) protein, and is currently being evaluated in the 30 mg every-eight-week (Q8W) multi-dose cohort of the Phase 1b/2a SELECT-HD clinical trial.
- In a non-human primate (NHP) study, WVE-003 achieved significant tissue exposure levels in deep brain regions, including the striatum. These data bolstered Wave's existing datasets that confirm the ability of its oligonucleotides to distribute to areas of the central nervous system associated with HD.
- WVE-003 has demonstrated single-dose reductions in mean cerebrospinal fluid mHTT of 35% compared to placebo, with preservation of wtHTT, as previously shared in September 2022.
- **Expected milestones:** Wave expects to report data from the 30 mg multi-dose cohort with extended follow-up, along with all single-dose data, in the second quarter of 2024. These data are expected to enable decision-making on the program and support the opt-in package for Takeda.

Cash runway

- Wave expects that its cash and cash equivalents, together with $115 million from its December 2023 offering and $27 million in recent collaboration milestones in the fourth quarter of 2023, will be sufficient to fund operations into the fourth quarter of 2025. Wave does not include future milestones or other contingent payments in its cash runway.

Upcoming events

- Paul Bolno, MD, MBA, President and Chief Executive Officer, is scheduled to present at the 42nd Annual J.P. Morgan Healthcare Conference in San Francisco, CA on Wednesday, January 10, 2024, at 3:00 p.m. PT / 6:00 p.m. ET. A live webcast of this presentation will be available on the Investor Relations page of the Wave Life Sciences website at http://ir.wavelifesciences.com. A replay of this presentation will be archived and available on the website for a limited time following the event.

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 ™, 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 concerning our goals, beliefs, expectations, strategies, objectives and plans, and other statements that are not necessarily based on historical facts, including statements regarding the following, among others: the anticipated initiation, site activation, patient recruitment, patient enrollment, dosing, generation of data and completion of our clinical trials, including any potential registration based on these data, and the announcement of such events; our expectations for 2024; our expectations to deliver the first-ever clinical proof-of-mechanism data for RNA editing, with WVE-006 in AATD, and our expectations for additional, wholly owned RNA editing programs; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; future preclinical activities and programs; regulatory submissions; the progress and potential benefits of our collaborations; the potential achievement of milestones under our collaborations and receipt of cash payments therefor; the potential of our preclinical data to predict the behavior of our compounds in humans; our identification and expected timing of future product candidates and their therapeutic potential; the anticipated benefits of our therapeutic candidates compared to others; our ability to design compounds using multiple modalities and the anticipated benefits of that approach; the breadth and versatility of PRISM™; the expected benefits of our stereopure oligonucleotides compared with stereorandom oligonucleotides; the potential benefits of our RNA editing capability, including our AIMers compared to others; the potential benefits of our GalNAc-conjugated siRNA program targeting INHBE; the status and progress of our programs relative to potential competitors; the benefit of nucleic acid therapeutics generally; the anticipated duration of our cash runway; our intended uses of capital; and our expectations regarding any potential global macro events beyond our control on our business. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the following: our ability to finance our drug discovery and development efforts and to raise additional capital when needed; the ability of our preclinical programs to produce data sufficient to support our clinical trial applications and the timing thereof; the clinical results of our programs and the timing thereof, which may not support further development of our product candidates; actions of regulatory authorities and their receptiveness to our adaptive trial designs, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing regulatory interactions and future clinical trials; the effectiveness of PRISM; the effectiveness of our RNA editing capability and our AIMers; our ability to demonstrate the therapeutic benefits of our candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our dependence on third parties, including contract research organizations, contract manufacturing organizations, collaborators and partners; our ability to manufacture or contract with third parties to manufacture drug material to support our programs and growth; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for the indications we are pursuing; our ability to maintain the company infrastructure and personnel needed to achieve our goals; and the information under the caption "Risk Factors" contained in our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and in other filings we make with the SEC from time to time. We undertake no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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