Wave Life Sciences Highlights Strategic Priorities and Expected 2025 Milestones Ahead of J.P. Morgan Presentation

January 13, 2025

Entering 2025 having demonstrated rapid translation of genetic insights to positive clinical data; advancing clinically validated and multi-modal pipeline with the potential to treat well over 100 million patients

CTAs submitted for Phase 1 INLIGHT clinical trial of WVE-007, a novel, long-acting, muscle-sparing GalNAc-siRNA approach for obesity targeting INHBE grounded in human genetics; proof-of-concept clinical data expected in 2025

Pioneering entirely new therapeutic field of RNA editing and building on positive WVE-006 proof-of mechanism clinical data; expect multidose AATD data, new preclinical data from hepatic and extra-hepatic RNA editing programs and candidate selections in 2025

Expect feedback from regulators and 48-week FORWARD-53 data for WVE-N531 in DMD in 1Q 2025; positive interim data demonstrated highly consistent dystrophin expression and best-in-class muscle delivery

Advancing WVE-003 – only allele-selective treatment for HD; planning underway for potentially registrational Phase 2/3 study with caudate atrophy as a primary endpoint and IND submission expected 2H 2025

Well-capitalized with expected runway into 2027

CAMBRIDGE, Mass., Jan. 13, 2025 (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 expected 2025 milestones across its clinical programs, growing pipeline, and leading RNA medicines platform ahead of the company's scheduled presentation at the 43 rd Annual J.P. Morgan Healthcare Conference in San Francisco, CA on Monday, January 13, 2025, at 9:45 a.m. PT / 12:45 p.m. ET.

"We delivered on key milestones across our pipeline in 2024, elucidating the potential of our best-in-class platform to advance transformative medicines. In 2025, we expect to continue this momentum as we advance our differentiated, high-impact clinical programs in DMD, HD and AATD and bring our innovative therapeutic approach for obesity into the clinic," said Paul Bolno, MD, MBA, President and Chief Executive Officer at Wave Life Sciences. "We are pioneering the RNA editing field with unmatched platform capabilities and a growing pipeline of innovative GalNAc programs for cardiometabolic diseases. We have also translated our best-in-class siRNA designs into a novel obesity candidate – WVE-007 – designed to go beyond weight loss to transform long-term cardiometabolic outcomes. Additionally, our DMD and HD programs continue to advance on their respective paths to potential registration in areas with immense unmet need and compelling market opportunities. We look forward to another transformative year for Wave, as we continue on our mission to unlock the broad potential of RNA medicines to improve the lives of patients and families."

2024 Achievements and 2025 Strategic Priorities

Advancing INLIGHT clinical study with novel, long-acting, muscle-sparing approach for obesity using Wave's best-in-class GalNAc-siRNA technology

- WVE-007 is a GalNAc-conjugated small interfering RNA (GalNAc-siRNA) that targets INHBE mRNA, an obesity target with strong evidence from human genetics. WVE-007 is Wave's first siRNA candidate to enter clinical development and uses Wave's best-in-class oligonucleotide chemistry.
- **Key achievements in 2024**
  - Wave shared preclinical data supporting WVE-007's potential to address multiple treatment settings, supporting potential broad use. In preclinical studies using a mouse model of diet induced obesity (DIO), a single dose of Wave's INHBE siRNA led to weight loss on par with semaglutide, with no muscle loss. When administered as an add-on to semaglutide, a single dose of Wave's INHBE siRNA doubled the amount of weight loss. In a third study, Wave's INHBE siRNA also prevented weight regain when semaglutide treatment was discontinued.
  - Since mid-December 2024, Wave has submitted multiple clinical trial applications (CTAs) for WVE-007 in obesity. This first-in-human Phase 1 clinical trial, "INLIGHT," is designed to enroll adults living with overweight or obesity to assess safety, tolerability, pharmacokinetics, biomarkers for target engagement, body weight and composition, and metabolic health, consistent with recently issued FDA draft guidance on developing therapeutics for weight reduction.
- **Expected upcoming milestones:**
  - Wave expects to initiate dosing in the INLIGHT clinical trial for WVE-007 in the first quarter of 2025 and to deliver proof-of-concept clinical data in 2025.
  - Proof-of-concept data are expected to include safety, tolerability, and biomarkers reflective of healthy weight loss.

Extending leadership in RNA editing led by WVE-006 for AATD and expanding GalNAc-AIMer pipeline

- WVE-006 is a GalNAc-conjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that is uniquely designed to address alpha-1 antitrypsin deficiency (AATD)-related lung disease, liver disease, or both.
- **Key achievements in 2024:**
  - Delivered proof-of-mechanism data from a single dose of WVE-006 from the first two patients in the RestorAATion-2 clinical trial of Pi*ZZ AATD patients, representing the first-ever clinical demonstration of RNA editing in humans. Mean total AAT protein increased to 10.8 micromolar, meeting the level that has been the basis

for regulatory approval for AAT augmentation therapies. Circulating wild-type M-AAT protein in plasma reached a mean of 6.9 micromolar, representing more than 60% of total AAT.
    - Completed multi-dosing of healthy volunteers in the top cohort in RestorAATion-1 at a dose level greater than those planned for any cohort of the RestorAATion-2 patient study.
    - Announced three wholly owned GalNAc-AIMer programs that offer first-in-class approaches to address unmet needs in cardiometabolic diseases. These new programs include PNPLA3, which aims to use mRNA correction for those at high risk for a variety of liver diseases, and LDLR and APOB, which utilize first-in-class mRNA upregulation and mRNA correction (respectively) to achieve target LDL-c levels in heterozygous familial hypercholesterolemia patients.
- **Expected upcoming milestones:**
    - Wave plans to share multidose data for WVE-006 from RestorAATion-2 in 2025.
    - Wave plans to share new preclinical data from its hepatic and extra-hepatic RNA editing programs in 2025.
    - Wave expects to initiate clinical development of additional RNA editing programs, including PNPLA3, LDLR, and APOB, in 2026.

Advancing DMD and HD clinical programs toward next milestones to unlock registrational opportunities
Duchenne Muscular Dystrophy (DMD)

- WVE-N531 is an exon skipping oligonucleotide designed to induce production of endogenous, functional dystrophin protein for the treatment of boys with DMD amenable to exon 53 skipping.
- **Key achievements in 2024**
    - Interim results of the Phase 2 FORWARD-53 study of WVE-N531 showed highly consistent, mean muscle content-adjusted dystrophin expression of 9.0% (range: 4.6-13.9%), best-in-class muscle delivery, multiple indicators of improved muscle health, and a safe and well-tolerated profile.
- **Expected upcoming milestones**:
    - The FORWARD-53 trial is ongoing and all patients have elected to continue treatment in the planned extension portion of the study with monthly doses of WVE-N531.
    - Wave expects to deliver the 48-week FORWARD-53 data and receive feedback from regulators on a pathway to accelerated approval in the first quarter of 2025.

Huntington's disease (HD)

- WVE-003 is a first-in-class, allele-selective oligonucleotide for the treatment of HD.
- **Key achievements in 2024:**
    - Results of the SELECT-HD clinical trial demonstrated the first-ever allele-selective reduction in CSF mutant huntingtin (mHTT) protein and preservation of healthy, wild-type huntingtin (wtHTT) protein with multiple doses of WVE-003, as well as a statistically significant correlation between mHTT reduction and slowing of caudate atrophy. By sparing wtHTT protein, which is critical to the health of the central nervous system, WVE-003 is uniquely positioned to address pre-symptomatic, as well as symptomatic, HD patients.
    - Wave received supportive initial feedback from FDA, who recognize the severity of HD and are receptive to and engaged with Wave regarding a potential pathway to accelerated approval. FDA is open to Wave's plan to evaluate biomarkers, including caudate atrophy, as an endpoint to assess HD progression with the potential to predict clinical outcome.
- **Expected upcoming milestones**:
    - Planning is underway for a global, potentially registrational Phase 2/3 study of WVE-003, including finalization of key aspects of design.
    - Wave expects to submit an Investigational New Drug ("IND") application for WVE-003 in the second half of 2025.

Cash runway

- Wave expects that its current cash and cash equivalents will be sufficient to fund operations into 2027. Potential future milestone and other payments to Wave under its GSK collaboration are not included in its cash runway.

Upcoming events

- Paul Bolno, MD, MBA, President and Chief Executive Officer, is scheduled to present at the 43rd Annual J.P. Morgan Healthcare Conference in San Francisco, CA today, Monday, January 13, 2025, at 9:45 a.m. PT / 12:45 p.m. ET. A live webcast of this presentation can be accessed by visiting "Investor Events" on the Investor Relations section of the Wave Life Sciences website: https://ir.wavelifesciences.com/events-publications/events. A replay of this presentation will be archived and available on the site 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 common 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 Alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy, Huntington's disease, and obesity, as well as several preclinical programs utilizing the company's broad RNA therapeutics toolkit. 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 and reporting of data and completion of our clinical trials, including interactions with regulators and any potential registration based on these data, and the timing and announcement of such events; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; our expectations with respect to how our clinical data successes to date may predict success for our future therapeutic candidates, future clinical data readouts and further validate of our platform; ongoing and future preclinical activities and programs, and their potential to transition into clinical-stage programs; the potential of our preclinical data to predict the behavior of our compounds in humans; regulatory submissions and timing for regulatory feedback; the progress and potential benefits of our collaborations; the potential achievement of milestones under our collaborations and receipt of cash payments therefor; the potential commercial opportunities that our therapeutic candidates may address; our identification and expected timing of future product candidates and their therapeutic potential; the anticipated benefits of our therapeutic candidates and pipeline compared to our competitors; patient population estimates related to our therapeutic candidates; our ability to design compounds using various modalities and the anticipated benefits of that approach; the breadth and versatility of our drug discovery and development platform; 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 for certain of our programs to be best-in-class or first-in-class; the status and progress of our programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; the benefits of RNA medicines generally; the strength of our intellectual property and the data that support our IP; the anticipated duration of our cash runway and our ability to fund future operations; our intended uses of capital; and our expectations regarding the impact of any potential global macro events 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 and accelerated approval pathways, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing regulatory interactions and future clinical trials; the effectiveness of our drug discovery and development platform; 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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