Wave Life Sciences Announces Positive Update on RestorAATion-2 Trial: WVE-006 (GalNAc-RNA Editing) Achieves MZ-Like Phenotype Across Both Biweekly and Monthly Dosing

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Data reinforce WVE-006's potential to address both lung and liver manifestations of AATD with a durable, convenient, and safe therapy capable of recapitulating the protective MZ-like phenotype with monthly dosing

On track for feedback from FDA on potential accelerated approval pathway mid-2026

WVE-006 generated wild-type M-AAT comprising 64% of total AAT and reduced harmful Z-AAT by 71%, with 11.9 µM total AAT in the 200 mg biweekly cohort; effects were consistent with 400 mg monthly dosing regimen, with 13.6 µM total AAT; editing was sustained at least three months following last dose

Restored dynamic AAT production with two new observations of elevated AAT during acute phase responses following mild upper respiratory infections, building on prior observation of 20.6 µM of total AAT during an acute phase response two weeks post-single 200 mg dose

RNA editing offers distinct safety advantages (reversible, no bystander edits or off-target edits) over DNA editing; WVE-006 continues to be generally safe and well tolerated with no liver toxicities

Wave to host investor webcast at 5:30 p.m. ET today

CAMBRIDGE, Mass., May 18, 2026 (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 updated data from the ongoing RestorAATion-2 trial of WVE-006, its investigational, GalNAc-conjugated, subcutaneously delivered RNA editing oligonucleotide (AIMer) for alpha-1 antitrypsin deficiency (AATD). These data further affirm WVE-006's potential as a novel therapeutic addressing both lung and liver AATD by generating healthy, wild-type M-AAT, reducing harmful Z-AAT, and restoring the ability to dynamically produce functional AAT protein when needed.

Individuals with Pi*ZZ AATD cannot produce healthy, wild-type M-AAT, have unhealthy, mutant Z-AAT aggregates in liver, and cannot dynamically increase AAT, a protein responsible for protecting lungs against ongoing damage. Heterozygous Pi*MZ individuals have low risk of lung or liver disease and circulating M-AAT levels ranging from 57% to 71% of total (mean=64%), based on analysis of natural history study samples measured with the same assay used in RestorAATion-2.

The only approved treatment for AATD is weekly intravenous plasma-derived augmentation therapy, which only addresses lung manifestations and may leave individuals living with AATD at risk if AAT protein levels fall too low during an acute phase response. There are no approved therapies for AATD liver disease.

"We have now seen consistent results across multiple cohorts that reaffirm WVE-006's potential to protect the liver by reducing the toxic Z-AAT protein, while simultaneously enabling a dynamic response capable of protecting the lung, especially during acute infections. RNA editing with WVE-006 offers distinct advantages compared to other treatment types. Our approach avoids delivery via lipid nanoparticles (LNPs), which have been associated with liver inflammation and dose-limiting toxicities. It also avoids the consequences associated with DNA base editing, including bystander edits, indels, and other off-target editing — permanent mutations in the human genome with unpredictable effects on gene expression," said Christopher Wright, MD, PhD, Chief Medical Officer at Wave Life Sciences. "Based on these data, we believe WVE-006 may offer a new standard of care that treats both lung and liver disease with convenient, infrequent subcutaneous dosing. We look forward to engaging with the FDA on our next phase of development."

Updated RestorAATion-2 clinical data
RestorAATion-2 is an ongoing open-label Phase 1b/2a trial with three dose cohorts (each n=8), with single and multidose portions. In the multidose portions, individuals receive multiple doses of WVE-006 (200 mg biweekly, 400 mg monthly, 600 mg monthly), over 12 weeks, followed by 12 weeks of follow-up. As of the data cutoff, data is available for the 200 mg (single and multidose), 400 mg (single and multidose), and 600 mg (single dose) cohorts. Circulating M-AAT, Z-AAT, and total (M + Z) AAT protein in the serum were measured by LC-MS/MS assays and reported as mean maximums.

Reductions in Z-AAT protein: In Pi*ZZ individuals, Z-AAT aggregates in the liver, where it can result in progressive liver disease. Treatment with WVE-006 led to robust, dose-dependent reductions of circulating, mutant Z-AAT from baseline following a single dose of WVE-006, reaching 47.3% (200 mg), 49.7% (400 mg), and 59.1% (600 mg). There were further reductions in Z-AAT with multiple doses of WVE-006, reaching 70.5% in the 200 mg biweekly dose cohort (seven doses). Reduction of Z-AAT was similar when extending the dosing interval, reaching 67.7% in the 400 mg monthly dose cohort (four doses).

Restoration of wild-type M-AAT protein: Individuals with Pi*ZZ AATD cannot produce wild-type M-AAT, the protein responsible for protecting the lungs against ongoing damage. Treatment with WVE-006 led to robust, dose-dependent restoration of wild-type M-AAT protein (canonical M-AAT) as a percentage of total circulating AAT following single doses of WVE-006, reaching 44.4% (200 mg), 48.0% (400 mg), and 52.3% (600 mg). In each single dose cohort, total AAT reached therapeutically relevant levels (200 mg: 12.9 µM; 400 mg: 14.0 µM; 600 mg: 13.0 µM). In the 200 mg multidose cohort, total AAT was 11.9 µM and M-AAT levels reached 64.4% of total AAT, in line with heterozygous MZ individuals with low risk of disease. A similar robust response was also observed when extending the dose interval to monthly (400 mg multidose cohort), where M-AAT levels reached 58.7% of total AAT. Total AAT in the 400 mg multidose cohort reached 13.6 µM.

Restoration of dynamic AAT protein: Notably, following treatment with WVE-006, three instances of dynamic and rapid production of AAT protein due to acute phase responses were observed across RestorAATion-2 as indicated by concurrent C-reactive protein (CRP) and AAT elevation. As previously reported, in the 200 mg single dose cohort, one individual produced a significant increase in total AAT (20.6 µM) following an acute phase response related to a kidney stone. In the 400 mg multidose cohort, there were two additional instances of significant increases in AAT (57.8% and 59.8% versus pre-event) following acute phase responses to mild upper respiratory infection (common cold). Additionally, across all available

RestorAATion-2 data to date, CRP increases are strongly correlated with increases in AAT (r=0.73, p<0.001, n=19).

Convenient dosing and strong safety: Data support monthly subcutaneous dosing, with editing sustained at least three months following the last dose in both the 200 mg and 400 mg multidose cohorts. WVE-006 continues to be well tolerated with a favorable safety profile to date. All adverse events (AEs) were mild to moderate in intensity, and there were no SAEs or clinically meaningful liver function test elevations.

D. Kyle Hogarth, MD, FCCP, Professor of Medicine, Director of the Alpha One Antitrypsin Deficiency Clinical Resource Center, Director of Bronchoscopy at the University of Chicago Medicine, commented: "This data represents another important development in the management of Alpha One. Being able to have the patient safely make their own M protein while decreasing their Z protein levels through a reversible approach that avoids permanent genomic modifications, and, importantly, restores dynamic AAT production to protect patients during acute phase response, is a major step forward for the Alpha One patient community."

Pavel Strnad, MD, Professor of Translational Gastroenterology and Senior Physician at the University Hospital Aachen, Department of Medicine III, commented: "AATD-associated liver disease is underdiagnosed, and individuals with the Pi*ZZ genotype are at risk for liver manifestations of disease including progressive fibrosis and cirrhosis, so it is essential that emerging therapies for AATD protect not only the lung but also the liver. The notable reductions in Z-AAT observed after treatment with WVE-006 suggest the potential to meaningfully reduce the toxic protein burden and reinforce the promise of RNA editing as a differentiated approach capable of delivering more complete care for people living with alpha-1. Beyond alpha-1, by correcting rather than silencing, these data demonstrate RNA editing's potential as an entirely new class of precision medicines to treat a range of genetic liver diseases."

Data from the RestorAATion-2 clinical trial were also highlighted earlier today at the American Thoracic Society (ATS) International Conference in an oral presentation by Kenneth R. Chapman, MsC, MD, FRCPC, FACP, FERS, Department of Medicine, University of Toronto.

Anticipated upcoming milestones for WVE-006

- Wave expects to receive regulatory feedback on a potential accelerated approval pathway mid-2026.
- Wave expects to share data from the 600 mg (monthly) multidose cohort in the second half of 2026.

Investor Conference Call and Webcast
Wave will host an investor conference call today at 5:30 p.m. ET to review the RestorAATion-2 program and updated clinical data. D. Kyle Hogarth, MD, FCCP, Professor of Medicine, Director of the Alpha One Antitrypsin Deficiency Clinical Resource Center, Director of Bronchoscopy at the University of Chicago Medicine, will provide a clinician perspective on AATD and treatment gaps. A webcast of the conference call 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. Analysts planning to participate during the Q&A portion of the live call can join the conference call at the audio-conferencing link 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 WVE-006
WVE-006 is a GalNAc-conjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that was developed with Wave's best-in-class oligonucleotide chemistry platform. By correcting the single RNA base mutation associated with the Pi*ZZ genotype, WVE-006 is designed to deliver a comprehensive treatment approach for AATD by producing healthy, wild-type M-AAT, decreasing unhealthy, mutant Z-AAT aggregates in liver, and dynamically increasing AAT, a protein responsible for protecting lungs against ongoing damage.

About RestorAATion-2
RestorAATion-2 (NCT06405633) is an ongoing Phase 1b/2a open label study designed to evaluate the safety, tolerability, pharmacodynamics, and pharmacokinetics of WVE-006 in individuals with AATD who have the homozygous Pi*ZZ mutation. The trial includes both single ascending dose and multiple ascending dose portions.

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, including RNAi (SpiNA) and RNA editing (AIMers), provides Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's pipeline is focused on its obesity (WVE-007), alpha-1 antitrypsin deficiency (WVE-006) and PNPLA3 I148M liver disease (WVE-008) programs, and also includes clinical programs in Duchenne muscular dystrophy and Huntington's disease, as well as several preclinical programs utilizing the company's versatile RNA medicines platform. 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 and LinkedIn.

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 understanding of the anticipated therapeutic benefits of WVE-006 as a therapy for AATD and the potential to address both lung and liver manifestations of the disease; our understanding of the levels of AAT considered to be therapeutically relevant; our understanding that treatment with WVE-006 enables the generation of healthy, wild-type M-AAT, reducing harmful Z-AAT, and restoring the ability to dynamically produce functional AAT protein when needed; our estimates of the AATD patient population that may benefit from WVE-006; our understanding of the dose levels and dosing frequency for WVE-006; our plans and estimated timing to share additional data from the RestorAATion-2 trial; anticipated interactions with and feedback from regulators and any potential regulatory submissions based on these data; our understanding of the safety profile of WVE-006; preclinical activities and programs and their potential to transition into clinical-stage programs, and the timing and announcement of data related to such activities; the potential benefits of our RNA editing capabilities, generally, and our understanding of the advantages of using RNA editing compared to other treatment types, including DNA editing; and our proprietary best-in-class chemistry. 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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