Correcting and Replacing Wave Life Sciences Announced Positive Target Engagement Data from INLIGHT Clinical Trial of WVE-007 for Obesity During Annual Research Day

October 29, 2025

This press release corrects and replaces the company's press release issued today, 10/29, at 4:15 p.m. ET in order to correct a typographical error in the first sub-bullet under "WVE-007 (GalNAc-siRNA)" – "Next steps."

Dose-dependent mean reductions of Activin E of up to 85% one month post single dose of WVE-007 in INLIGHT clinical trial, exceeding levels that led to weight loss in preclinical models; WVE-007 is generally safe and well tolerated to date

Activin E reduction in lowest dose cohort of INLIGHT was sustained through 6 months, supporting once or twice a year dosing

Multiple clinical data updates from INLIGHT, including body composition and body weight, are anticipated starting in 4Q 2025

Additional updates included announcement of WVE-008, PNPLA3 RNA editing candidate for liver disease, with CTA submission anticipated in 2026

Preclinical data supports Wave's emerging pipeline of hepatic and extra-hepatic RNA editing and siRNA programs; emerging modality adds capability to simultaneously edit and silence two unique targets with a single oligonucleotide construct

CAMBRIDGE, Mass., Oct. 29, 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 Activin E target engagement data from its INLIGHT clinical trial of WVE-007, a GalNAc-siRNA, for the treatment of obesity during the company's annual analyst and investor Research Day.

"We are incredibly excited to be observing potent, durable, and dose-dependent Activin E reductions with just single doses of WVE-007 in the first three cohorts of our INLIGHT clinical trial for obesity. This indicates our preclinical data are translating and affirms we have a potential best-in-class RNAi modality enabled by our proprietary chemistry, including PN," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We also continue to lead the field in RNA editing. With the successful clinical translation of WVE-006 for AATD, we are further expanding our editing pipeline and have now selected WVE-008 as our PNPLA3 RNA editing clinical candidate for liver disease. WVE-008 is on track to enter clinical development next year with the filing of a CTA. In addition to that, we are pioneering a new modality by uniting editing and silencing in a single oligonucleotide construct. With multiple planned clinical updates across our RNA editing and RNAi programs, Wave is in a unique position to unlock tremendous value from our robust RNA medicines pipeline."

INLIGHT clinical study and target engagement update:

WVE-007 (GalNAc-siRNA): *INHBE silencing approach designed to reduce fat while preserving muscle mass*

- Wave's INHBE program has a strong foundation in human genetics. People living with naturally low levels of INHBE have lower levels of unhealthy visceral fat, lower fasting glucose and triglycerides, and a lower risk of type 2 diabetes and cardiovascular disease. Silencing INHBE mRNA aims to reduce Activin E levels, thereby inducing fat loss without impacting muscle mass.
- In Wave's preclinical studies of mice with diet-induced obesity (DIO), single doses of GalNAc INHBE-siRNA led to potent and durable Activin E reductions of greater than 70%, and weight loss driven by reduction in visceral fat, without affecting muscle mass. Preclinical studies also support the use of INHBE GalNAc-siRNA as an add-on to GLP-1s or to curtail weight regain following cessation of GLP-1s. These reduced Activin E levels led to adipocyte shrinkage, fewer pro-inflammatory macrophages, less fibrosis, and improved insulin sensitivity in visceral adipose tissue, linking increased lipolysis to lower cardiometabolic risk.
- Today, Wave announced highly significant, dose-dependent Activin E reductions were observed in the first three cohorts of its ongoing INLIGHT clinical trial evaluating WVE-007 (3:1 active: placebo). The trial is designed to address safety and tolerability as well as target engagement (Activin E reduction). One-month follow-up was available from Cohort 2 (240 mg) and Cohort 3 (400 mg), and six-month follow-up from Cohort 1.
- At day 29 (one month post single dose), mean Activin E reductions from baseline were all highly significant ($p<0.0001$ for all doses):
    - Cohort 3 (400 mg): 85% reduction
    - Cohort 2 (240 mg): 75% reduction
    - Cohort 1 (75 mg): 56% reduction
- The one-month reductions of Activin E observed in the 240 mg and 400 mg cohorts exceed levels that led to fat loss in preclinical models.
- In Cohort 1 (75 mg), Activin E reductions were durable throughout the 6-month follow-up, supporting WVE-007's potential for once or twice yearly doing.
- WVE-007 is safe and well tolerated to date. An independent data monitoring committee supported dose expansion of the 600 mg cohort and dose escalation beyond that.
- WVE-007 aims to achieve fat loss on par with semaglutide by six months of follow up post-single WVE-007 dose.
- **Next steps:** Wave expects to deliver multiple clinical data updates from INLIGHT, including body composition and body weight:
    - **4Q 2025:** anticipated three-month follow-up data from the expanded Cohort 2 (240 mg), as well as data from Cohort 1 (75 mg).
    - **1Q 2026:** anticipated six-month follow-up data from Cohort 2 and three-month follow-up data from Cohort 3.
    - **2Q 2026:** anticipated six-month follow-up data from Cohort 3 and three-month follow-up data from Cohort 4.

Additional details can be found in the company's Research Day presentation.

Additional updates from today's presentation:

WVE-006 (RNA Editing): *potential first- and best-in-class therapy for AATD that addresses both lung and liver manifestations of the disease*

- The ongoing Phase 1b/2a RestorAATion-2 study is evaluating WVE-006, a GalNAc-conjugated RNA editing oligonucleotide, as a treatment for alpha-1 antitrypsin deficiency (AATD). The multidose portion of Cohort 2 is currently ongoing with monthly doses of 400 mg. Today, Wave announced Cohort 3 is now underway at doses of 600 mg of WVE-006.
- In September 2025, Wave announced WVE-006 has already achieved key treatment goals by restoring protein levels associated with lower risk of AATD liver and lung diseases. Total AAT levels reached 13 µM, wild-type M-AAT protein accounted for 64% of circulating total AAT after treatment, with a corresponding reduction in Z-AAT. Notably, WVE-006 restored the ability to dynamically produce therapeutically relevant levels of AAT protein during an acute phase response, with an individual reaching over 20 µM AAT protein.
- **Next steps:** 400 mg multidose cohort data expected in the first quarter of 2026; 600 mg single dosing is underway in the third and final cohort, with single and multi-dose data expected in 2026.

WVE-008 (RNA Editing): *potential first-in-class, disease modifying therapy for PNPLA3-I148M liver disease*

- Building on the successful clinical translation of Wave's RNA editing capability, the company has selected WVE-008 as its clinical candidate for PNPLA3-I148M liver disease.
- There are an estimated 9 million homozygous PNPLA3-I148M individuals with liver disease in the U.S. and Europe. These homozygous carriers have a significantly higher risk of liver-related death compared to heterozygous carriers. Wave's RNA editing approach aims to achieve at least 50% correction to restore the heterozygous phenotype with low risk of liver disease, similar to the approach with WVE-006.
- **Next steps:** Wave expects to file a Clinical Trial Application (CTA) for WVE-008 in 2026.

Wave's platform innovations: *extra-hepatic delivery and an emerging new modality*

- Through chemistry optimization tailored to target and cell type, Wave is expanding its emerging pipeline of siRNAs (SpiNAs) and RNA editing oligonucleotides (AIMers) to both hepatic and extrahepatic tissues, including skeletal muscle, heart, adipose, and kidney.
- Emerging modality adds capability to simultaneously edit and silence two unique targets with a single oligonucleotide construct. Wave presented preclinical data demonstrating that a single GalNAc-oligonucleotide construct upregulated LDLR protein and silenced PCSK9 mRNA.

An archived webcast of the event 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.

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, obesity, Duchenne muscular dystrophy, and Huntington's disease, 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 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; our understanding of the dose levels and dosing frequency of our therapeutic candidates; our understanding of the safety profile of our therapeutic candidates; our expectations for our clinical candidates and the anticipated therapeutic benefits thereof; the potential of WVE-007's mechanism (INHBE) as a novel and unique obesity treatment to induce fat loss, preserve muscle, and drive weight loss; 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 anticipated therapeutic benefits of WVE-008 as a therapy for PNPLA3-I148M liver disease; regulatory submissions and timing for regulatory feedback; 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 preclinical and clinical data successes to date may predict success for our future therapeutic candidates, future clinical data readouts and further validate of our platform; 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 clinical-stage programs 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 and the potential addressable market that our therapeutics may address; our ability to design compounds using various modalities and the anticipated benefits of that approach; the breadth and versatility of our PRISM 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 benefits of our emerging pipeline of siRNAs (SpiNAs) compared to others; the benefits of RNA medicines generally; the potential for certain of our programs to be best-in-class or first-in-class; our ability to translate genetic insights into high impact medicines; the status and progress of our programs relative to potential competitors; the progress and potential benefits of our collaborations; our expectations on the company's future growth; and the anticipated duration of our cash runway and our ability to fund future operations. 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 results to 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.

Contact:
Kate Rausch
VP, Corporate Affairs and Investor Relations
+1 617-949-4827

Investors:
James Salierno
Director, Investor Relations
+1 617-949-4043
InvestorRelations@wavelifesci.com

Media:
Katie Sullivan
Senior Director, Corporate Communications
+1 617-949-2936
MediaRelations@wavelifesci.com

Source: Wave Life Sciences USA, Inc.