Wave Life Sciences to Present Preclinical Data Supporting Therapeutic Potential of WVE-007 for Obesity at ObesityWeek® 2025

November 4, 2025

Presentation will highlight preclinical data supporting the potential of WVE-007 (INHBE GalNAc-siRNA) as a unique approach for the treatment of obesity designed to drive fat loss while preserving muscle mass with once or twice annual dosing

In preclinical models, INHBE GalNAc-siRNA led to adipocyte shrinkage, fewer pro-inflammatory macrophages, less fibrosis, and improved insulin sensitivity in visceral adipose tissue, supporting potential for metabolic improvement

As an add-on to semaglutide, Wave's GalNAc-siRNA doubled weight loss in mice and prevented weight regain upon cessation of semaglutide

INLIGHT clinical study evaluating WVE-007 is ongoing: last week Wave announced positive target engagement, including dose-dependent decreases in Activin E (up to 85%) observed one month post-single dose of WVE-007, exceeding the reductions seen in preclinical models that led to weight loss; highly durable reductions persisted through six-month follow-up; safe and well tolerated profile

CAMBRIDGE, Mass., Nov. 04, 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 the presentation of the company's preclinical data supporting WVE-007, its GalNAc-siRNA investigational therapeutic for obesity. The data will be highlighted on November 6 in a poster presentation at ObesityWeek®, the annual congress of The Obesity Society, in Atlanta.

WVE-007 is a GalNAc-siRNA designed to reduce fat while preserving lean mass by silencing INHBE mRNA, an obesity target with strong evidence from 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.

"With a strong foundation in human genetics, WVE-007 is focused on healthy weight loss driven by fat loss, in particular visceral fat loss, while preserving muscle to make meaningful improvements in cardiometabolic health, which is ultimately the main objective of any obesity medication. GLP-1 receptor agonists have transformed obesity care, but their impact is often limited by tolerability, frequent dosing, and perhaps most importantly, loss of muscle mass," said Erik Ingelsson, MD, PhD, Chief Scientific Officer of Wave Life Sciences. "WVE-007 is currently advancing in the INLIGHT clinical study and we announced exciting target engagement data last week, with dose-dependent and durable Activin E reductions observed in the first three dose cohorts, exceeding levels that led to weight loss in our preclinical models. We are particularly encouraged by the durability of silencing observed, which suggests our investigational therapy may only need to be dosed once or twice per year."

ObesityWeek® poster presentation information:

Title: Targeting Adipose Lipolysis with INHBE Silencing Promotes a Healthy Weight Loss Profile in Mice (Poster-710)

Presenter: Ginnie (Hsiu-Chiung) Yang, PhD, SVP, Translational Medicine, Wave Life Sciences

Date and Time: November 6, 2025, 2:30-3:30pm ET

Location: Georgia World Congress Center (GWCC), Building A, 285 Andrew Young International Blvd NW, Atlanta, GA 30313

Wave investigated the impact of the company's GalNAc-conjugated siRNA designed to lower the expression of INHBE mRNA in a diet-induced obesity (DIO) mouse model.

Key results are as follows:

- A single dose of Wave's GalNAc-conjugated INHBE-siRNA in mice led to statistically significant weight loss compared to placebo (PBS treatment), reductions in visceral adipose fat mass and adipocyte size compared to controls, and no loss of skeletal muscle mass, suggesting Wave's treatment induces a healthy weight loss comprised of fat loss and preservation of lean mass.
- Wave's treatment led to decreased infiltration of total and pro-inflammatory macrophages by up to 41% and 80%, respectively, and reduced fibrosis by 58% in visceral adipose tissue of DIO mice. These changes align with lower risk of cardiovascular disease and type 2 diabetes.
- When added to semaglutide, Wave's GalNAc INHBE-siRNA doubled weight loss in mice and reduced weight regain upon cessation of semaglutide.

The full presentation can be accessed on the Wave Life Sciences website here.

Recent clinical progress for WVE-007:

Last week at its Research Day, Wave shared Activin E target engagement data from its ongoing, first-in-human INLIGHT clinical trial (3:1 active: placebo). One-month follow-up was available from Cohort 2 (240 mg) and Cohort 3 (400 mg), and six-month follow-up was available from Cohort 1 (75 mg). Highly significant ($p<0.0001$ for all doses), dose-dependent mean Activin E reductions from baseline were observed at Day 29 (one month post single dose) in the first three cohorts: 85% reduction (Cohort 3), 75% reduction (Cohort 2), 56% reduction (Cohort 1), exceeding reductions that led to weight loss in preclinical models. In Cohort 1, Activin E reductions were durable throughout the six-month follow-up, supporting WVE-007's potential for once or twice yearly doing.

WVE-007 was safe and well-tolerated to date. An independent data monitoring committee supported dose expansion of Cohort 4 (600 mg) and dose escalation beyond that.

Wave expects to deliver multiple near-term clinical data updates from INLIGHT, including body composition and body weight, beginning with three-month follow-up data from the Cohort 2 (240 mg) and data from Cohort 1 (75 mg) in the fourth quarter of 2025, six-month follow-up data from Cohort 2 (240 mg) and three-month follow-up data from Cohort 3 (400 mg) in the first quarter of 2026, and six-month follow-up data from Cohort 3 (400 mg) and three-month follow-up data from Cohort 4 (600 mg) in the second quarter of 2026.

Additional details can be found in the company's Research Day presentation from October 29, 2025.

About INLIGHT
INLIGHT is an ongoing, first-in-human clinical trial (3:1 active: placebo) evaluating WVE-007 in adults living with overweight or obesity and assesses safety, tolerability, pharmacokinetics, biomarkers for target engagement, body weight and composition, and metabolic health. Key inclusion criteria include A1c of less than 5.9 and BMI between 28 and 35. The lowest dose cohort of 75 mg enrolled eight participants. The subsequent cohorts (Cohorts 2, 3, and 4) were expanded to 32 subjects. An independent data monitoring committee has also approved further escalation to a next higher dose in Cohort 5.

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 within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding our plans to present and discuss our preclinical data supporting WVE-007 for obesity at ObesityWeek®; our expectations for WVE-007 and the anticipated therapeutic benefits thereof; the anticipated timing of clinical data from our INLIGHT clinical trial of WVE-007; the novelty of our approach to silence INHBE mRNA in order to achieve healthy, sustainable weight loss and the potential for once- or twice-yearly dosing in light of the significant durability of the Activin E reductions observed in INLIGHT; the potential benefits of WVE-007 over existing obesity therapies; 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; our understanding of our preclinical data for WVE-007 and our expectations of how such data will translate in humans, including the ability to make meaningful improvements in cardiometabolic health, the main objective of any obesity; our understanding of the safety profile of WVE-007; beliefs that Wave's portfolio of RNA medicines is differentiated, potentially best-in-class and potentially transformative; the broad potential of Wave's RNA medicines pipeline and oligonucleotide chemistry and any benefits that may arise as a result thereof. 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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