Wave Life Sciences Announces Initiation of Phase 2a Portion of INLIGHT™ Trial of WVE-007 (INHBE GalNAc-siRNA) for Obesity and Cardiometabolic Diseases

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In Phase 1 portion of trial, WVE-007 improved body composition by inducing fat loss, including harmful visceral fat, while maintaining muscle; data continue to support once or twice-yearly dosing

Phase 2a portion in individuals with higher BMI and body fat, with and without type 2 diabetes, includes multiple assessments to inform further development of WVE-007 in obesity as well as MASH, type 2 diabetes, and cardiovascular disease

Wave is on track to initiate additional Phase 2 trials in 2H 2026 evaluating WVE-007 in combination with incretins and as post-incretin maintenance

CAMBRIDGE, Mass., June 24, 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 it has initiated the Phase 2a multidose portion of the INLIGHT™ trial, a placebo-controlled (3:1) study evaluating WVE-007, an investigational GalNAc-siRNA, as monotherapy in individuals living with obesity with high BMI (35-50 kg/m^2) and comorbidities.

The INLIGHT trial also includes an ongoing Phase 1 single dose portion investigating WVE-007 in otherwise healthy individuals living with overweight or obesity, with an average BMI of 32 kg/m^2. In this portion of the trial, at six months of follow-up, a single 240 mg dose of WVE-007 continued to drive clinically meaningful reductions in visceral fat (-14%; $p<0.05$), total fat (-5%), and waist circumference (-3%). WVE-007 continues to be generally safe and well tolerated up to 600 mg and data support the potential for once or twice-yearly dosing. The Phase 2a portion of the INLIGHT trial is expected to demonstrate further body composition improvements, including greater fat loss with preserved muscle, weight loss, and improved biomarkers of cardiometabolic health.

“We have strong conviction in WVE-007’s potential to redefine obesity treatment and long-term cardiometabolic health, with early clinical results demonstrating a 14% visceral fat reduction without muscle loss six months following a single dose. The link between visceral fat and cardiometabolic outcomes is well established and further validated by a recent publication which demonstrated that for every 10% reduction in visceral fat, an individual’s risk of developing type 2 diabetes was 28% lower even a decade later,” [1] said Christopher Wright, MD, PhD, Chief Medical Officer at Wave Life Sciences. “Importantly, this next portion of the INLIGHT trial will evaluate a patient population with higher BMI and greater adiposity, consistent with Phase 2 and Phase 3 obesity trials. Given WVE-007’s mechanism of targeted lipolysis, we believe this portion of the study can deliver even more pronounced improvements in body composition and we expect to gain a clearer understanding of WVE-007's potential to drive clinically meaningful weight loss, reduce fat, and preserve muscle, while informing its broader role in metabolic care.”

The Phase 2a portion of the INLIGHT trial is expected to enroll participants across the U.S. and Europe and includes multiple assessments over a 12-month period, including body weight, waist circumference, body composition (MRI and DEXA), liver fat (MRI-PDFF), HbA1c, and lipid levels. The results will inform further development of WVE-007 in obesity, as well as MASH, type 2 diabetes, and cardiovascular disease.

Wave also expects to initiate new clinical trials evaluating WVE-007 as an incretin add-on and as post-incretin maintenance in the second half of 2026.

About WVE-007
WVE-007 is an investigational GalNAc-siRNA that utilizes Wave’s best-in-class proprietary oligonucleotide chemistry and the company’s Stereopure interfering Nucleic Acid (SpiNA) next generation siRNA design. WVE-007 is designed to silence INHBE mRNA, an obesity target with strong evidence from human genetics. Individuals who have a protective loss-of-function variant in one copy of the INHBE gene have a healthier body composition and cardiometabolic profile, including less visceral fat and lower risk of type 2 diabetes or cardiovascular disease. 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.

About the INLIGHT™ Clinical Trial
The INLIGHT trial is an ongoing randomized, placebo-controlled (3:1) study that includes a Phase 1, single-ascending dose portion in otherwise healthy individuals living with overweight or obesity. This portion is designed to assess safety, tolerability, pharmacokinetics, and Activin E target engagement. The INLIGHT trial is currently ongoing at multiple trial sites, including in the U.S. A Phase 2a portion of the INLIGHT trial is evaluating multiple WVE-007 doses in individuals with high BMI, with and without type 2 diabetes, and will assess metabolic and body composition improvements as well as weight loss.

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 PRISM® platform combines multiple RNA medicines 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 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/or completion of our ongoing and anticipated Phase 2 portions of our INLIGHT clinical trial and the timing and announcement of such events; our expectations to initiate new clinical trials evaluating WVE-007 as an incretin add-on and as post-incretin maintenance, and the expected results and timing thereof; our understanding of the dose levels

and dosing frequency for WVE-007; our understanding of the safety profile for WVE-007; the potential of WVE-007's mechanism (INHBE GalNAc-siRNA) as a meaningful and differentiated therapeutic approach for obesity as well as the potential to develop WVE-007 for other indications, including MASH, type 2 diabetes, and cardiovascular disease; the protocol, design and endpoints of the Phase 2a portion of our INLIGHT clinical trial; the future performance and results of WVE-007 in the Phase 2a portion of our INLIGHT clinical trial, including our expectations that there will be even greater improvements in body composition in individuals with higher BMI, visceral fat and body fat at baseline, with and without type 2 diabetes; the potential benefits of our toolkit of RNA-targeting modalities, including RNAi (SpiNA) and RNA editing (AIMers), compared to others; the benefits of RNA medicines generally; and the potential for certain of our programs to be best-in-class. 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.

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[1] Klein, Hadar, Liav Alufer, Dana Tamar Goldberg Toren, et al. *Circulation,* 2026 June 2. "Lifestyle-Induced Visceral Fat Loss as a Key Target for Durable Cardiometabolic Health: MRI-Assessed 5- and 10-Year Follow-Up After 2 Clinical Trials."