Wave Life Sciences Announces Positive Interim Phase 1 Data from INLIGHT: Further Improvements in Body Composition, with Clinically Meaningful Reductions in Visceral Fat and Waist Circumference, at Six Months Following Single Dose of WVE-007

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At 6-month follow-up, a single 240 mg dose of WVE-007 (INHBE GalNAc-siRNA) continued to drive significant placebo-adjusted reductions in visceral fat (-14%; p<0.05) and total fat (-5%), stabilization of lean mass (+2%), and reductions in waist circumference (-3%) and body weight (-1%)

WVE-007 led to greater improvement in body composition (visceral fat-to-muscle ratio) at six months versus that seen with weekly GLP-1 in later-stage trial (BMI: ~37 kg/m^2), even with participants in Phase 1 portion of INLIGHT™ having substantially lower BMI (~32 kg/m^2) and lower levels of fat than those in Phase 2 and 3 obesity studies

Phase 2a portion of INLIGHT in individuals with higher BMI (35-50 kg/m^2) and comorbidities expected to demonstrate further body composition improvements and weight loss; data will inform further development in obesity as well as MASH, type 2 diabetes, and cardiovascular disease; on track to initiate in 2Q 2026

Durable and dose-dependent suppression of serum Activin E sustained through at least seven months continues to support expectations for once or twice-yearly dosing

WVE-007 continues to be generally safe and well tolerated

Investor conference call and webcast at 8:30 a.m. ET today

CAMBRIDGE, Mass., March 26, 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 new data from the Phase 1 portion of its first-in-human INLIGHT trial evaluating WVE-007, an investigational INHBE GalNAc-siRNA (SpiNA design), in otherwise healthy individuals living with overweight or obesity. After six months of follow-up, a single 240 mg dose led to further improvements in body composition, including fat loss with muscle preservation, with clinically meaningful reductions in visceral fat and waist circumference in a population with less fat and lower BMI than those in Phase 2 and 3 obesity studies.

"WVE-007 is already translating in the clinic with potent and durable Activin E reductions and it continues to be safe and well tolerated. Even in this early Phase 1 trial, we are seeing our differentiated chemistry translate into clinically meaningful levels of fat loss, particularly harmful visceral fat, with muscle preservation. What's remarkable is that these results were observed in participants who have a substantially lower BMI and less fat than those typically enrolled in later-stage obesity studies, six months after only a single dose," said Christopher Wright, MD, PhD, Chief Medical Officer at Wave Life Sciences. "Our analysis suggests there will be even greater improvement in individuals with higher BMI in the Phase 2a portion of INLIGHT, including more pronounced visceral and total fat loss with similar lean mass preservation, thus inducing greater weight loss. Additionally, WVE-007 could serve as a particularly meaningful therapeutic option for those vulnerable to muscle loss, and those currently taking GLP-1s who are looking for a long-term maintenance strategy. Beyond obesity, by significantly lowering visceral fat and retaining skeletal muscle, today's data also suggest WVE-007's powerful, differentiated cardiometabolic profile could address additional indications such as MASH, type 2 diabetes, and cardiovascular disease. The Phase 2a portion of INLIGHT is designed to inform these additional opportunities."

Compelling human genetic data support targeting INHBE as a therapeutic approach for obesity and improved cardiometabolic health. Silencing INHBE and its downstream gene product, Activin E, induces fat loss through lipolysis, the breakdown of triglycerides directly in adipocytes, without reducing muscle. A reduction in visceral fat of 5-10% is associated with a significantly lower risk of developing MASH, type 2 diabetes, and cardiovascular disease. Preservation of muscle is a key differentiator from incretin treatments and muscle is linked to health benefits including higher basal metabolic rate, improved insulin sensitivity, and prevention of weight regain.

Phase 1 (SAD) portion of INLIGHT
In the 240 mg cohort, six-month data demonstrated further improvements in body composition following a single dose of WVE-007, with statistically significant reductions in visceral fat and clinically meaningful reductions in waist circumference, as well as reductions in body weight. There were 32 participants in the 240 mg cohort (3:1 treatment to placebo) that had an average BMI of 32 kg/m^2 and less visceral and subcutaneous fat than those in Phase 2 or 3 obesity studies.

Placebo-adjusted percent change from baseline*		***240 mg 3-month follow-up***	***240 mg 6-month follow-up***
DEXA	Visceral fat mass	-7.8%	-14.3% (p<0.05)
	Total fat mass	-5.1%	-5.3%
	Lean mass	+2.2%	+2.4%
Clinical measurements	Waist circumference	-0.4%	-3.3%
	Body weight	-0.3%	-0.9%

**The results were analyzed with a pre-specified statistical analysis (MMRM) utilizing all available data across all timepoints and dose groups at the time of the current data analysis and utilizing a pooled placebo comparator.*

The improvement in body composition as measured by visceral fat-to-muscle ratio (VMR) observed with a single 240 mg dose of WVE-007 (-16.5% vs. baseline) in the Phase 1 INLIGHT trial was greater than that achieved with weekly 2.4 mg doses of semaglutide at six months (-12.2% vs. baseline) in the BELIEVE Phase 2 clinical trial, which enrolled a higher BMI population (average 37 kg/m²). VMR is an established measure of body composition integrating harmful visceral fat and beneficial lean mass into a single index. Lower VMR is associated with a decreased risk of MASH, type 2 diabetes, and cardiometabolic disorders.

Consistent, durable, and dose-dependent serum Activin E reductions sustained through at least seven months continue to support WVE-007's potential for once or twice-yearly dosing, with a mean maximum reduction of up to 88%.

WVE-007 continues to be generally safe and well tolerated to date up to 600 mg**.** There were no treatment discontinuations, and no severe or serious treatment emergent adverse events (TEAEs). All TEAEs in the treatment groups were mild or moderate, and all treatment-related adverse events were mild. There were no clinically meaningful changes in clinical laboratory measurements, including lipid profiles or liver function tests.

400 mg three-month data
In the 400 mg cohort, three-month data demonstrated placebo-adjusted reductions in visceral fat (-5.0%), total fat (-0.7%), with lean mass preservation (-0.2%) from baseline following a single dose. Notably, the 400 mg cohort had a leaner baseline body composition, with lower BMI and more participants (10 out of 24 individuals) with healthy levels of visceral fat (≤500 g). A post-hoc analysis of the three-month results demonstrated a more robust and statistically significant average reduction in visceral fat (-7.8%, $p<0.05$) in individuals with higher baseline visceral fat (>500g), similar to that observed in the 240 mg cohort. These results emphasize the impact of baseline body composition on therapeutic effect and support expectations that evaluating individuals with higher BMI and visceral fat at baseline will lead to greater improvements in body composition and weight loss.

Phase 2a high BMI (MAD) portion of INLIGHT
Wave is on track to initiate the Phase 2a multidose portion of INLIGHT evaluating WVE-007 as monotherapy in individuals with higher BMI (35-50 kg/m^2) and comorbidities in the second quarter of 2026. This placebo-controlled (3:1) Phase 2a study will include multiple assessments over a 12-month period, including body weight, waist circumference, body composition (MRI and DEXA), liver fat (MRI-PDFF), HbA1c, lipid levels, CRP, and muscle function. The study is expected to demonstrate further body composition improvements, including greater fat loss with preserved muscle, and additional weight loss. The results will inform further development of WVE-007 in obesity, as well as MASH, type 2 diabetes, and cardiovascular disease. The first assessment in this portion of the trial is planned for three months after participants have received their first dose.

"It is exciting to see WVE-007's unique effect on fat loss with muscle preservation. These data are highly encouraging especially given the profound impact on visceral fat and impressive reduction in waist circumference—both of which are tied to meaningful clinical outcomes—following just a single dose. As physicians, we need to set expectations around what healthy weight loss looks like, and visceral fat-to-muscle ratio allows us to focus patients on the measurements that matter," said Angela Fitch, MD, FACP, co-founder and Chief Medical Officer at knownwell, former co-director of the Massachusetts General Hospital Weight Center, faculty at Harvard Medical School, and former president of the Obesity Medicine Association. "My patients want to know their waist circumference is going down along with their visceral fat, and they are worried about any loss of muscle. This data update reinforces Wave's potential with WVE-007 to deliver a meaningful and differentiated tool in our clinical toolbox."

Anticipated upcoming WVE-007 milestones
Additional data from INLIGHT, including data from the 600 mg Phase 1 SAD cohort, are expected in 2026.

Wave expects to initiate the Phase 2a multidose portion of INLIGHT in individuals with higher BMI and comorbidities in the second quarter of 2026 and initiate new clinical trials evaluating WVE-007 as an incretin add-on and as post-incretin maintenance in 2026.

Investor Conference Call and Webcast
Wave will host an investor conference call today at 8:30 a.m. ET to review the INLIGHT Phase 1 interim clinical data. 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-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
INLIGHT is an ongoing randomized, placebo-controlled (3:1) clinical trial that includes a Phase 1, single-ascending dose portion in otherwise healthy individuals living with overweight or obesity. This portion is designed to address safety, tolerability, pharmacokinetics, and Activin E target engagement. INLIGHT is currently ongoing at multiple trial sites, including in the US. A Phase 2a portion of INLIGHT evaluating multiple WVE-007 doses in individuals with high BMI and comorbidities is expected to initiate in the second quarter of 2026.

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 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 the Phase 2a portion 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; 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 body composition improvements in individuals with higher BMI and visceral fat at baseline; our expectations with respect to how our preclinical data for WVE-007 may predict its behavior in humans, predict success for our future therapeutic

candidates, future clinical data readouts and further validate of our platform; 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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