WAVE® LIFE SCIENCES

Positive Interim Clinical Data from INLIGHT Trial of WVE-007 in Obesity

Investor Presentation

December 8, 2025

Forward-looking statements

This document contains forward-looking statements. All statements other than statements of historical facts contained in this document, including statements regarding possible or assumed future results of operations, preclinical and clinical studies, business strategies, research and development plans, collaborations and partnerships, regulatory activities and timing thereof, competitive position, potential growth opportunities, use of proceeds and the effects of competition are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause the actual results, performance or achievements of Wave Life Sciences Ltd. (the "Company") to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. The Company has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that it believes may affect the Company's business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including those listed under Risk Factors in the Company's Form 10-K and other filings with the SEC, some of which cannot be predicted or quantified and some of which are beyond the Company's control. The events and circumstances reflected in the Company's forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, the Company operates in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that the Company may face. Except as required by applicable law, the Company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Today's agenda

Opening remarks
Paul Bolno, MD, MBA
President and CEO

WVE-007: INHBE GalNAc-siRNA for obesity
Erik Ingelsson, MD, PhD
Chief Scientific Officer

INLIGHT interim clinical data
Chris Wright MD, PhD
Chief Medical Officer

Opportunity for WVE-007 and next steps
Paul Bolno, MD, MBA
President and CEO

Q&A

Opening remarks

Paul Bolno, MD, MBA

President and CEO

WAVE LIFE SCIENCES

Single dose of WVE-007 led to improvement in body composition with fat loss similar to GLP-1 at 3 months without muscle loss

Positive interim data from Phase 1 INLIGHT, 3-month follow-up from 240 mg SAD cohort

Improved body composition vs. baseline, with **reduction in total body fat** (-4.5%, p=0.07), including **visceral fat loss** (-9.4%, p=0.02)

Preservation of muscle with a 3.2% increase in lean mass (p=0.01)

Potent and durable serum Activin E reductions

Generally **safe and well tolerated**

Transformative potential of WVE-007

- **Similar fat loss to GLP-1, without muscle loss**
- **Continued improvements in body composition with once or twice-yearly dosing**
- **Favorable safety and tolerability profile**

WAVE LIFE SCIENCES

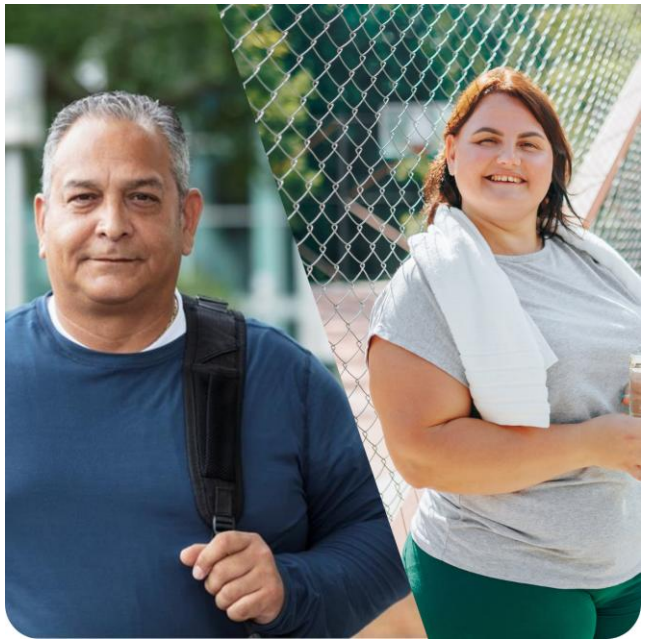
All DEXA percentage changes and p-values are model-based, using the SAP pre-specified analysis; p-values are from tests of within-group change over time; no p values were statistically significant for placebo; SAD: single-ascending dose

WVE-007: INHBE GalNAc-siRNA for obesity

Erik Ingelsson, MD, PhD
Chief Scientific Officer

WAVE LIFE SCIENCES

Obesity is a metabolic disease in need of a treatment paradigm shift



- Individuals living with **obesity** have higher risk for many serious health conditions, including heart disease, type 2 diabetes, and some forms of cancer[1]
- **GLP-1s** are current standard of care for weight loss, but impact is often limited by:
  - Loss of muscle mass[2]
  - Poor tolerability[3]
  - Frequent dosing[4]
  - High discontinuation rates[5,6]

> 1 billion people living with obesity globally

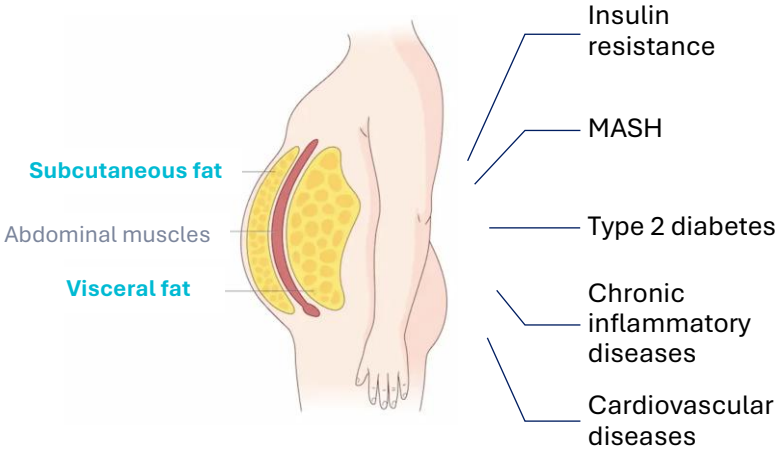
Improving body composition is the future of obesity therapeutics

1. Koenen et al. 2021 Circ Res 128, 951; 2. Sargeant, et al. 2019 Endocrinol Metab (Seoul) 34, 247; 3. Ghusn and Hurtado. 2024 Obesity Pillars 12, 100127; 4. Wegovy PI; 5. Leach, et al. 2023 Prime Therapeutics Claims Analysis; 6. Gasoyan, et al. 2024 Obesity (Silver Spring) 32, 486.

Body composition improvements: Reducing fat, including visceral fat, while also preserving lean mass

Reduce fat, including visceral fat

Increased visceral adiposity is associated with many diseases including cardiometabolic disorders



Preserve lean mass, including muscle

- Maintaining metabolic rate
- Improved insulin sensitivity
- Prevent weight regain
- Preserve muscle strength and function
- Reduce frailty

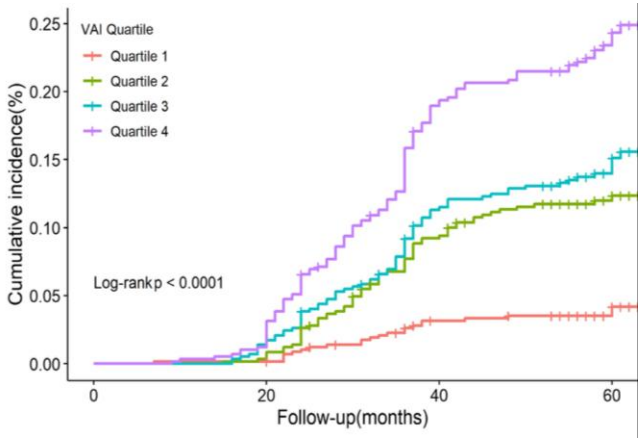
1. Liao, Y. *et al.* 2025 *Front. Nutr.* 11, 1517186; 2. Ibarra-Reynoso, L.d.R. *et al.* 2025 *J. Clin. Med.* 14, 8365; 3. Wu, Q-W., *et al.* 2025 *Front. Endocrinol.* 16, 1635282; 4. Galvan, B. *et al.* 2025 J. *Funct. Morphol. Kinesiol.* 10, 244. MASH: Metabolic Dysfunction Associated Steatohepatitis

Visceral fat is associated with insulin sensitivity and incidence of MASH, type 2 diabetes and cardiovascular disease

Visceral fat reduction is associated with multiple health benefits

Health Outcome	Visceral Fat Reduction	Associated Benefits
Insulin Sensitivity[1]	≥ 5% decrease in visceral fat	Improved insulin sensitivity, lower HbA1c, better lipid profile
Cardiovascular Risk[2]	≥ 5–10% decrease in visceral fat	Reduced blood pressure, improved lipids, lower systemic inflammation
Liver Fat (Steatosis)[3]	≥ 10% decrease in visceral fat or ≥ 7–10% body weight loss	Significant reduction in hepatic triglycerides, improved liver enzymes
Hepatic Fibrosis[4]	≥ 10% decrease in visceral fat or ≥ 7–10% body weight loss	Resolution of steatohepatitis in up to 90%, fibrosis regression in many cases

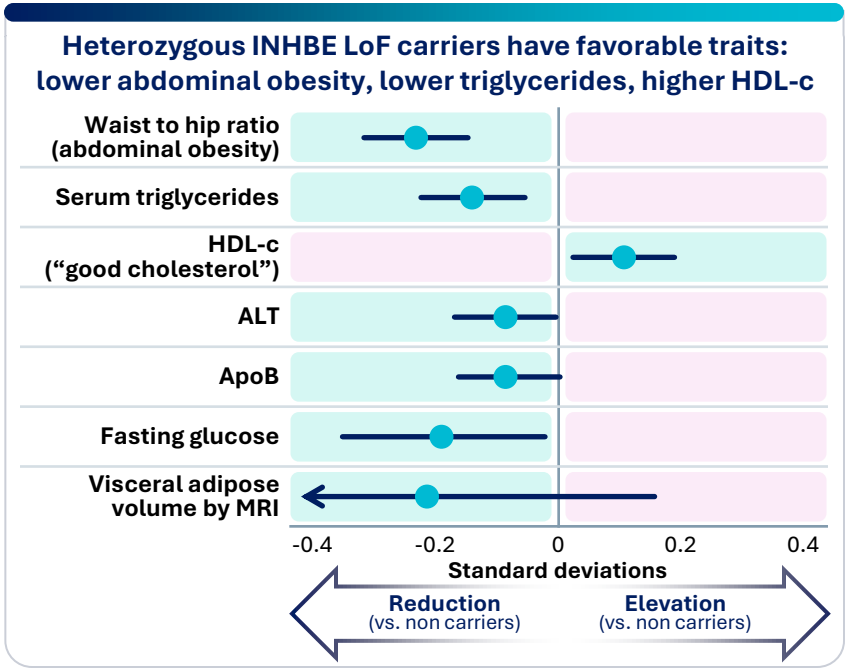
Visceral fat increases risk of cardiovascular disease[5]

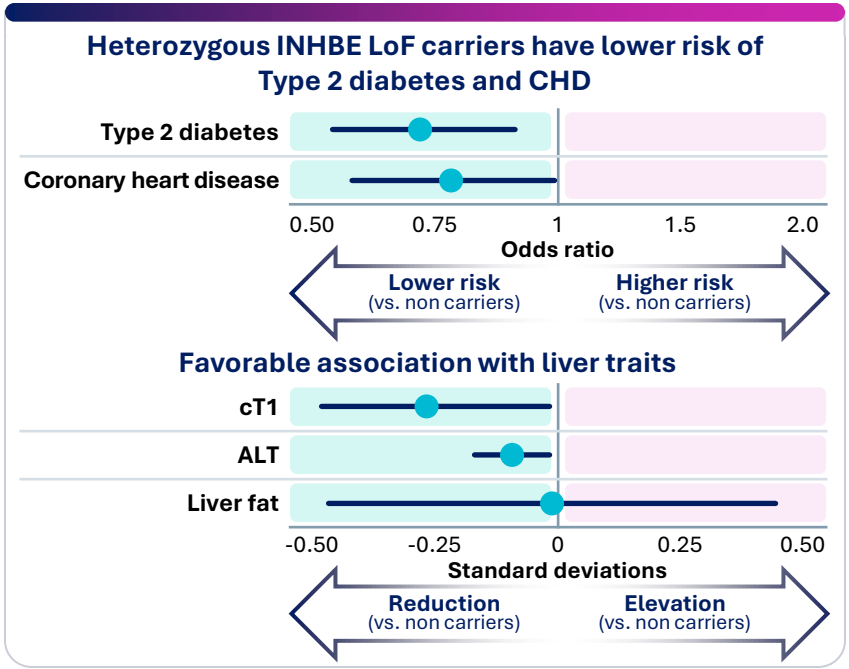


WVE-007 aims to shift body composition by reducing body fat while preserving muscle, to deliver a healthier cardiometabolic profile

1. Gabriely et al., *Diabetes* 2002; Campos et al., *Diabetes & Vascular Disease Research* 2019; Huang et al., *Front Endocrinol* 2023. 2. Cesaro et al., Front Cardiovasc Med 2023; Khawaja et al., Curr Cardiol Rep 2024; Hiuge-Shimizu et al., J Atheroscler Thromb 2011. 3. Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020; Hanlon & Yuan, Clin Liver Dis 2021. 4. Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020. 5. Kouli et al., *Nutr Metab Cardiovasc* Dis. 2017. Qaio et al. *Cardiovasc Diabetol* 21, 225 (2022). VAI = Visceral Adiposity Index

Human genetic data demonstrate that heterozygous INHBE loss-of-function (LoF) carriers have a healthy metabolic profile





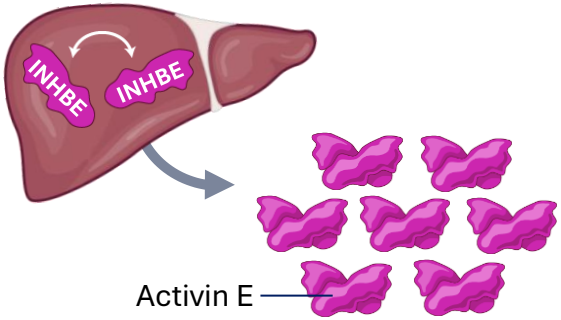
Silencing INHBE mRNA by ≥50% is expected to recapitulate the healthy metabolic profile of heterozygous INHBE LoF carriers

Akbari et al. *Nat Commun*. 2022 Aug 23;13(1):4844; Deaton et al. *Nat Commun*. 2022 Jul 27

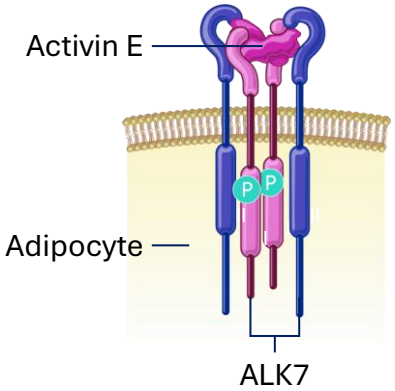
Waist to hip ratio: waist to hip ratio adjusted for BMI; HDL-c: high-density lipoprotein cholesterol; ALT: alanine transaminase; ApoB: apolipoprotein B; CHD: coronary heart disease; cT1: corrected T1

Silencing INHBE mRNA is expected to drive lipolysis without appetite suppression and corresponding muscle loss

Release of **dimerized** INHBE subunits creates hepatokine **Activin E**



Binds to and **activates** **ACVR1C** (ALK7) receptor in adipose tissue



Blocking adipose lipolysis

Increased abdominal adiposity leads to **obesity, CVD and T2D**

1. Cell Reports (2018) 25, 1193–1203; 2. Biochemical Journal (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8

Treatment with WVE-007 (SpiNA GalNAc-siRNA) is expected to drive fat reduction and improve key measures of cardiometabolic health

Leading siRNA design (SpiNA)[1]

WVE-007
(INHBE GalNAc-siRNA)

- Proprietary, clinically validated chemistry
- Subcutaneous injection (GalNAc)
- Potential for infrequent dosing (1 – 2x year)

Driving fat reduction

Reduction of INHBE mRNA and circulating Activin E

- **Adipocyte lipolysis** ↑
- **Adipocyte size** ↓
- **Proinflammatory macrophages in adipose** ↓
- **Fibrosis** ↓
- **Insulin sensitivity** ↑

And improving clinical outcomes

Cardiometabolic outcomes

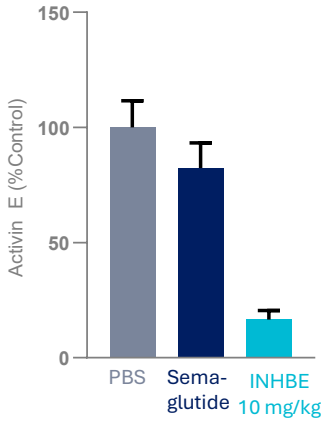
- ↓ Risk of CVD
- ↓ Risk of T2D

1. SpiNA design is derived from Liu et al., 2023 Nucleic Acids Research doi: 10.1093/nar/gkad268

Single dose of INHBE GalNAc-siRNA led to durable Activin E reductions, and sustained improvements in body composition in DIO mice

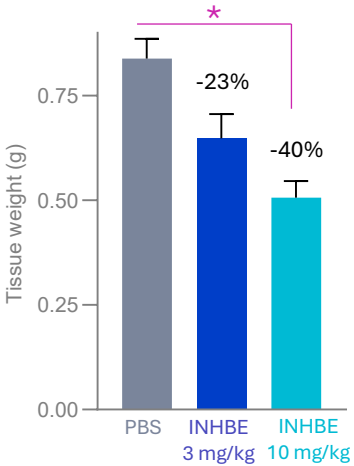
Durable Activin E reduction

Serum Activin E



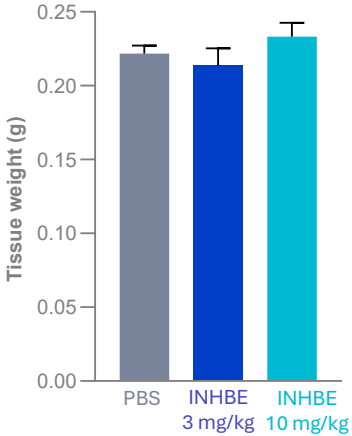
Reduction in fat

Epididymal fat weight



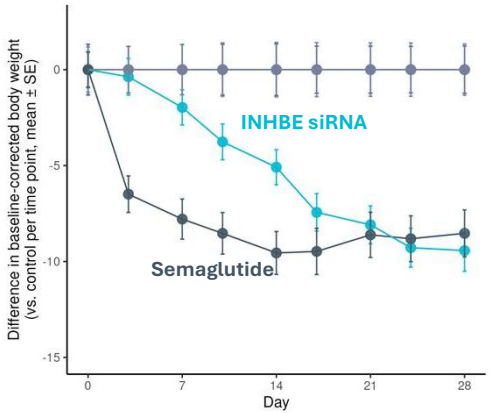
Muscle preservation

Quadricep weight



Reduction in body weight

Single dose INHBE GalNAc-siRNA



Left and right panels: Semaglutide 10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human; INHBE GalNAc-siRNA 10 mg/kg dose. All data from preclinical studies were conducted in mice fed with 60% high fat diet. Linear Mixed Effects ANOVA with post hoc comparisons of marginal treatment effects vs. PBS per tissue.* $p < 0.05$

INLIGHT interim clinical data

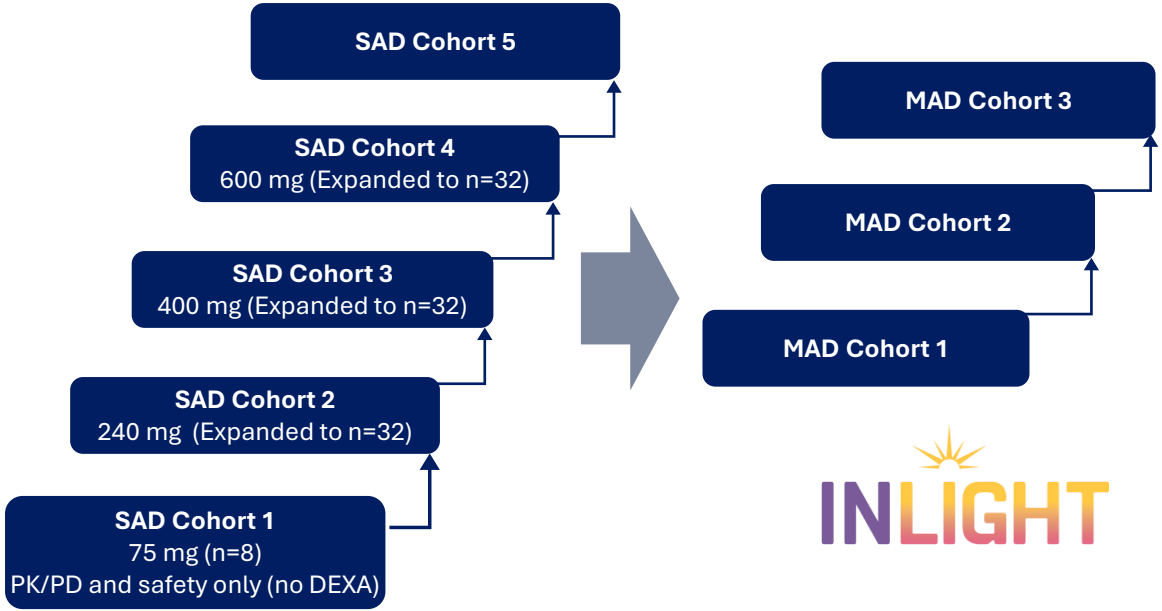
Chris Wright, MD, PhD
Chief Medical Officer

WAVE LIFE SCIENCES

INLIGHT: Phase 1 clinical trial in otherwise healthy individuals living with overweight or obesity

Randomized, double-blind, placebo-controlled (3:1) study of ascending doses of WVE-007

- **Objective**: Assess dose safety, tolerability, PK and PD
- **Key study criteria:**
  - **HbA1c:** <5.9
  - **BMI:** 28 – 35 kg/m^2 (SAD)
- **Key measurements:**
  - **Primary:** Safety and tolerability
  - **Secondary:** PK, Activin E
  - **Exploratory PD:**
    - Body composition (DEXA)
    - Biomarkers
    - Body weight
- Multiple clinical trial sites, including US



No diet or exercise modifications are instituted in this trial, following the standard practice

SAD: single-ascending dose; MAD: multi-ascending dose; PK: pharmacokinetics; PD: pharmacodynamics

Baseline participant characteristics were similar across cohorts

INLIGHT Baseline Participant Characteristics	Placebo N=10	WVE-007 75 mg N=6	WVE-007 240 mg N=24
Age at consent (years)	36.4 (8.2)	38.3 (3.7)	40.5 (11.2)
Gender, Male Female	 5 (50.0) 5 (50.0)	 2 (33.3) 4 (66.7)	 15 (62.5) 9 (37.5)
Weight (kg)	94.0 (13.6)	97.4 (15.5)	97.7 (17.0)
Total fat mass (kg)	32.6 (3.2)	NA	34.2 (9.0)
Lean mass (kg)	58.6 (11.1)	NA	58.4 (10.8)
Visceral fat mass (kg)	0.7 (0.4)	NA	1.0 (0.6)
BMI (kg/m^2)	31.5 (2.5)	32.5 (2.8)	32.1 (2.9)

All values are mean (SD) or N (%). Total fat mass, lean mass and visceral fat mass were measured by DEXA in the 240 mg cohort. Lean mass equals tissues excluding bone and fat. Visceral fat is measured in the android region

INLIGHT: WVE-007 continues to be generally safe and well tolerated

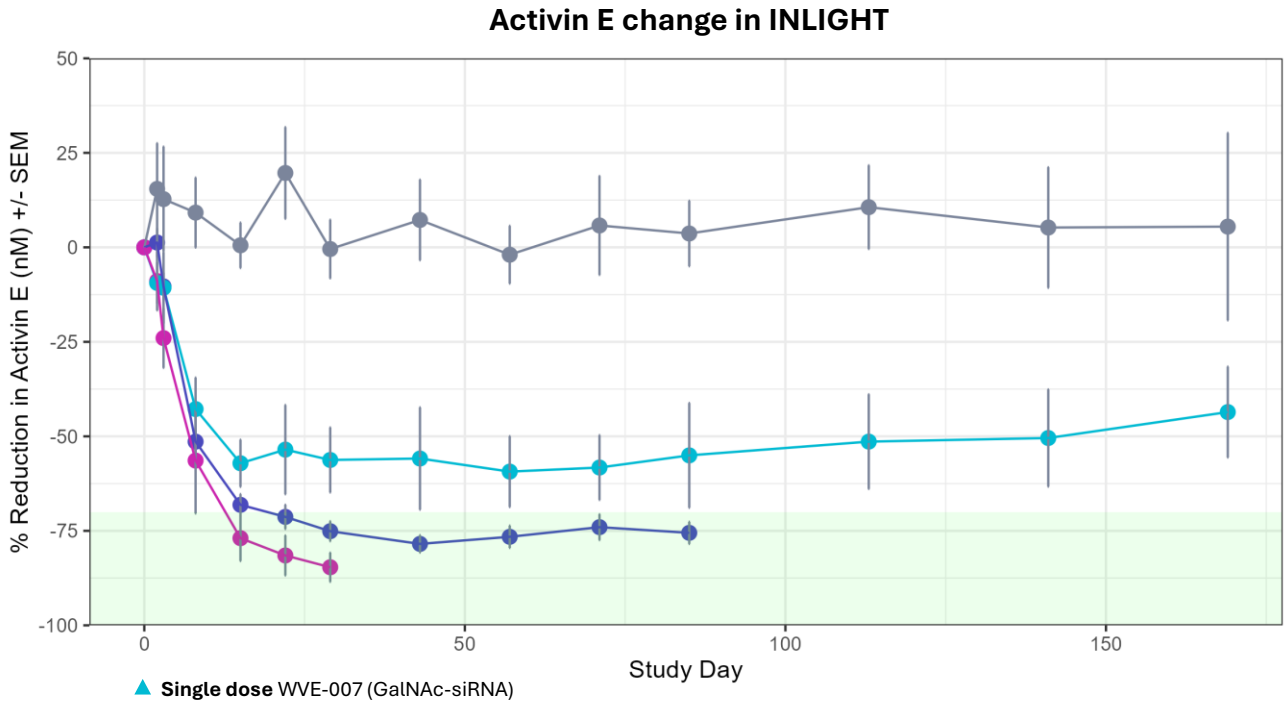
TEAE Category	Placebo N=26 n (%)	75 mg N=6 n (%)	240 mg N=24 n (%)	400 mg N=24 n (%)	600 mg N=23 n (%)
Any TEAE	10 (38.5)	3 (50.0)	19 (79.2)	15 (62.5)	9 (39.1)
Mild	5 (19.2)	2 (33.3)	14 (58.3)	10 (41.7)	8 (34.8)
Moderate	4 (15.4)	1 (16.7)	5 (20.8)	5 (20.8)	1 (4.3)
Severe	1 (3.8)	0	0	0	0
Any drug-related TEAE	2 (7.7)	1 (16.7)	8 (33.3)	9 (37.5)	6 (26.1)
Mild	2 (7.7)	1 (16.7)	8 (33.3)	9 (37.5)	6 (26.1)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
Any serious TEAE	0	0	0	0	0
Any TEAE leading to discontinuation	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0

- No discontinuations, serious TEAEs, or deaths
- All study treatment-related AEs were mild
- No clinically meaningful changes in lipids or other clinical laboratory measurements including LFTs

Generally safe and well tolerated through 600 mg

Data as of December 2, 2025; TEAE: treatment-emergent adverse event; LFT: liver function test

Highly durable, dose dependent, serum Activin E reductions with WVE-007 supporting dosing once or twice per year

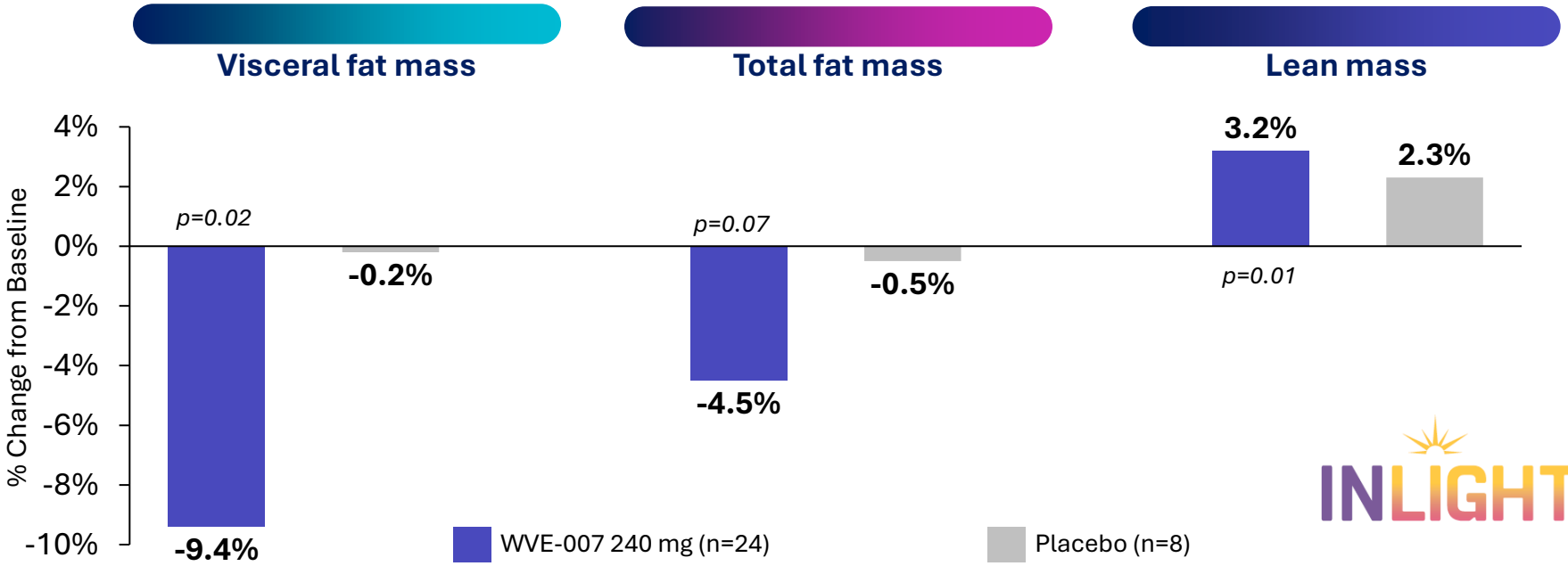


INLIGHT

Dose	Max Activin E reduction
Placebo (n=13)	
WVE-007 75 mg (n=6)	-59%
WVE-007 240 mg (n=24)	-78%
WVE-007 400 mg (n=6)	-85%

Figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. Placebo includes one individual from 400 mg expansion.
Green shading: >70% Activin E reductions in preclinical models led to fat loss

Reductions in visceral and total fat mass with preservation of lean mass observed at three months in INLIGHT after a single WVE-007 dose



INLIGHT

Potential for best-in-class obesity treatment profile with improvement in body composition

WAVE LIFE SCIENCES

All DEXA percentage changes and p-values are model-based, using the SAP pre-specified analysis; p-values are from tests of within-group change over time; no p values were statistically significant for placebo.

Single dose of WVE-007 led to improvements in body composition with fat loss similar to GLP-1 at three months without muscle loss

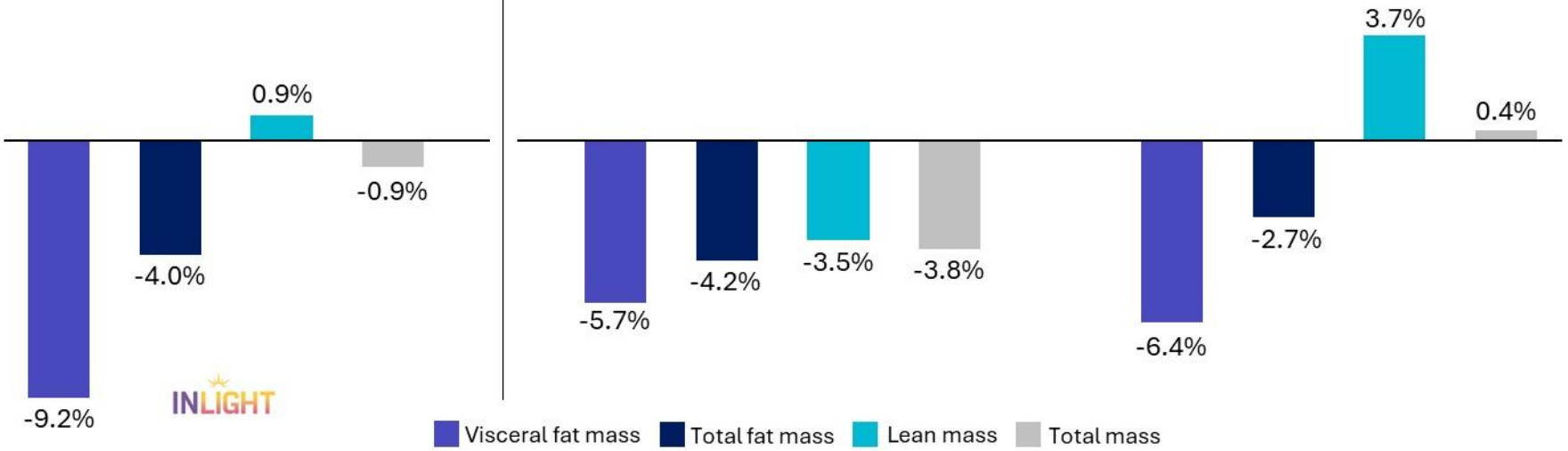
INLIGHT Phase 1 Trial
Placebo-adj. values at 12 weeks[1]

WVE-007 (INHBE GalNAc-siRNA)
Single dose; 240 mg
Mean BMI: 32.1 kg/m^2
No diet/exercise modifications

BELIEVE Phase 2 Trial
Placebo-adj. estimated values at 12 weeks[2]

Semaglutide (GLP-1 agonist)
Weekly[3]; 2.4 mg
Mean BMI: 36.6 kg/m^2
With diet/exercise modifications

Bimagrumab (myostatin inhibitor)
2 doses[4]; 10 mg/kg
Mean BMI: 36.5 kg/m^2
With diet/exercise modifications



1. For INLIGHT, all DEXA percentage changes and p-values are model-based, using the SAP pre-specified analysis. 2. For BELIEVE, all data points are approximate and based on placebo-adjusted estimates extracted from figures, body weight reported as total mass, from Heymsfield SB, et al. Symposium – "*Can we improve the quality of weight loss by augmenting fat mass loss while preserving lean mass? The BELIEVE study of bimagrumab + semaglutide*". Presented at: American Diabetes Association Scientific Sessions; June 20-23, 2025; Chicago. 3. Semaglutide in BELIEVE study was subcutaneously administered weekly and titrated to maintenance dose. N=57 in semaglutide 2.4 mg arm, N=56 in placebo arm. 4. Within the first 12 weeks of the BELIEVE study, bimagrumab was dosed IV at baseline and week 4. N=56 in bimagrumab 10 mg/kg arm, N=56 in placebo arm. **Note: The data presented above are derived from different clinical trials with differences in trial design and patient population, including with respect to BMI. As a result, cross-trial comparisons cannot be made and no head-to-head clinical trials have been conducted.**

WAVE® LIFE SCIENCES

Opportunity for WVE-007 and next steps

Paul Bolno, MD, MBA

President and CEO

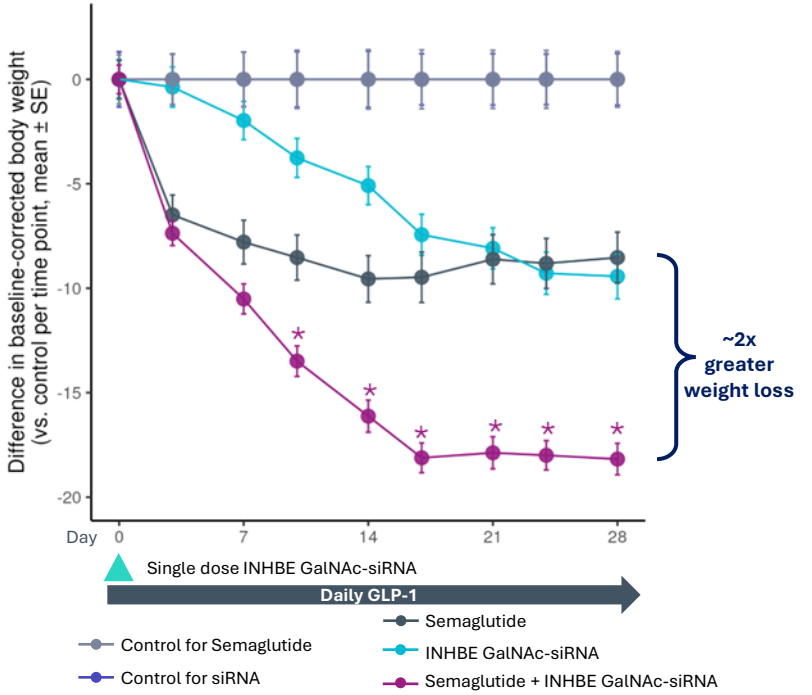
WAVE LIFE SCIENCES

WVE-007: Potentially transformative profile to improve body composition and change obesity treatment paradigm

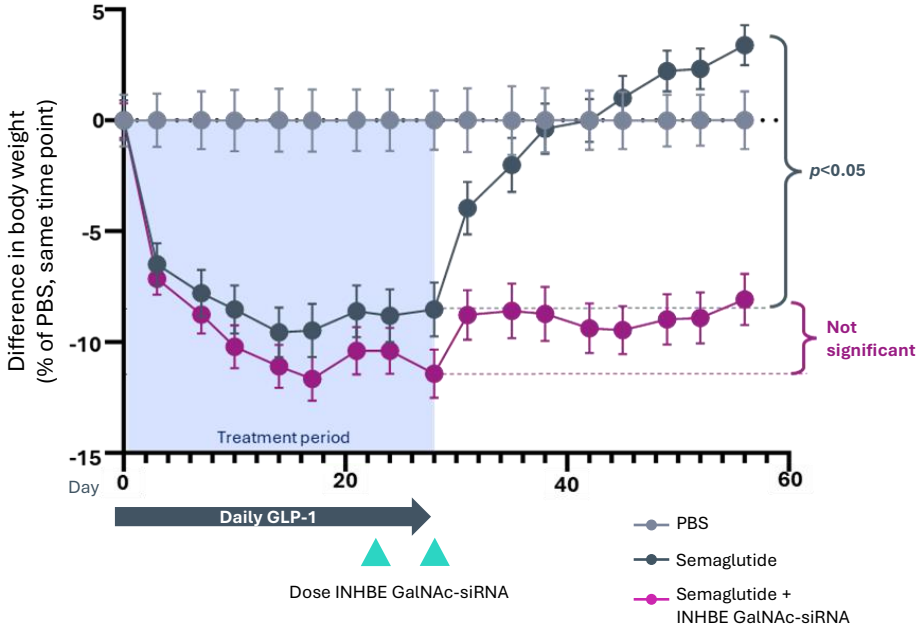
- Reduces fat mass through lipolysis
- Preserves muscle
- Once or twice-yearly dosing
- Favorable safety and tolerability profile

WVE-007 has potential for use synergistically with GLP-1s or to curtail weight regain after the cessation of treatment with GLP-1, based on preclinical data

Combined with GLP-1: Greater weight loss



After cessation of GLP-1: Curtails weight re-gain



Data from preclinical studies conducted in mice fed with 60% high fat diet; Left: semaglutide10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human. Left Stats: Linear Mixed Effects ANOVA with post hoc comparisons of marginal treatment effects of Semaglutide vs. Semaglutide + INHBE GalNAc-siRNA per time point * $p < 0.05$; Right Stats: Linear Mixed Effects ANOVA with post hoc comparison of Day 28 vs. Day 56 marginal effects per treatment

Planning underway for Phase 2 trials evaluating WVE-007 across multiple treatment settings

Monotherapy

In higher BMI patient populations with or without cardiometabolic comorbidities

- To induce fat loss with muscle preservation and favorable safety and tolerability

Add-on

Add-on to incretin treatments

- To leverage an orthogonal mechanism to incretins for enhanced efficacy

Maintenance

An off-ramp post-incretin treatments

- To prevent weight rebound and maintain metabolic improvements upon incretin cessation

Potential to address > 1 billion individuals living with obesity globally

Near term anticipated data updates for WVE-007

1Q26

- **6-month** follow-up data from the **240 mg** single-dose cohort
- **3-month** follow-up data from the **400 mg** single-dose cohort

2Q26

- **6-month** follow-up data from the **400 mg** single-dose cohort
- **3-month** follow-up data from the **600 mg** single-dose cohort

Longer follow-up and higher dose cohorts expected to deliver further fat loss

Thank you to the participants, families, clinicians and study site staff who are participating in this study

WAVE® LIFE SCIENCES

Reimagine possible.

For questions contact:
investorrelations@wavelifesci.com