Positive Interim Phase 1 Clinical Data from INLIGHT Trial of WVE-007 for Obesity

Investor Presentation

March 26, 2026

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 Phase 1 data and Phase 2a update
Christopher 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

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Today's update: WVE-007 Interim Phase 1 clinical data demonstrates further improvements in body composition

INLIGHT™

Phase 1 otherwise healthy (SAD)
Lower BMI of ~32 kg/m^2

Improved body composition six months following single 240 mg dose:

- Significant reduction in **visceral fat** (-14%*)
- Reduction in **waist circumference** (-3%)
- Reduction in **total fat** (-5%)
- Stabilization of **lean mass** (+2%)
- Reduction in **body weight** (-1%)

- 400 mg three-month data emphasize impact of baseline body composition on therapeutic effect
- **Durable and dose-dependent** suppression of Activin E sustained through at least 7 months continues to support **1-2x yearly dosing**
- **Generally safe and well tolerated**

Phase 2a high BMI and comorbidities (MAD)
BMI of 35-50 kg/m^2

On track to initiate in 2Q 2026

- Expect greater improvements in body composition and weight loss
- Key endpoints include body composition (DEXA and MRI), liver fat (MRI-PDFF), HbA1c, lipid levels, CRP, and muscle function
  - Inform further development in obesity, as well as MASH, type 2 diabetes, and cardiovascular disease

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*p<0.05. All reductions are placebo-adjusted % change from baseline were estimated using an MMRM model with fixed effects for treatment group, visit, treatment-by-visit interaction, and baseline as a covariate; estimates were based on geometric mean ratios.

WVE-007: INHBE GalNAc-siRNA for obesity

Erik Ingelsson, MD, PhD
Chief Scientific Officer

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WVE-007 (investigational INHBE GalNAc-siRNA) is a potentially transformative approach for the > 1 billion people living with obesity globally

Significant unmet need in obesity

Current standard of care: Focused on caloric restriction by reducing appetite and slowing gastric emptying

Incretins limited by:

- Muscle loss[1]
- Frequent dosing[2]
- Poor tolerability[3]
- High discontinuation rates[4,5]

Resulting in need for therapies that can:

- Induce **fat loss** with **muscle preservation**
- Leverage **orthogonal mechanism** for **enhanced** efficacy and **maintain metabolic improvements** after incretin cessation

WVE-007

Focused on adipocyte lipolysis and not caloric deficit

- **Drives total and visceral fat loss**
- **Preserves muscle**
- **Potential 1–2x per year dosing**
- **Generally safe and well tolerated**

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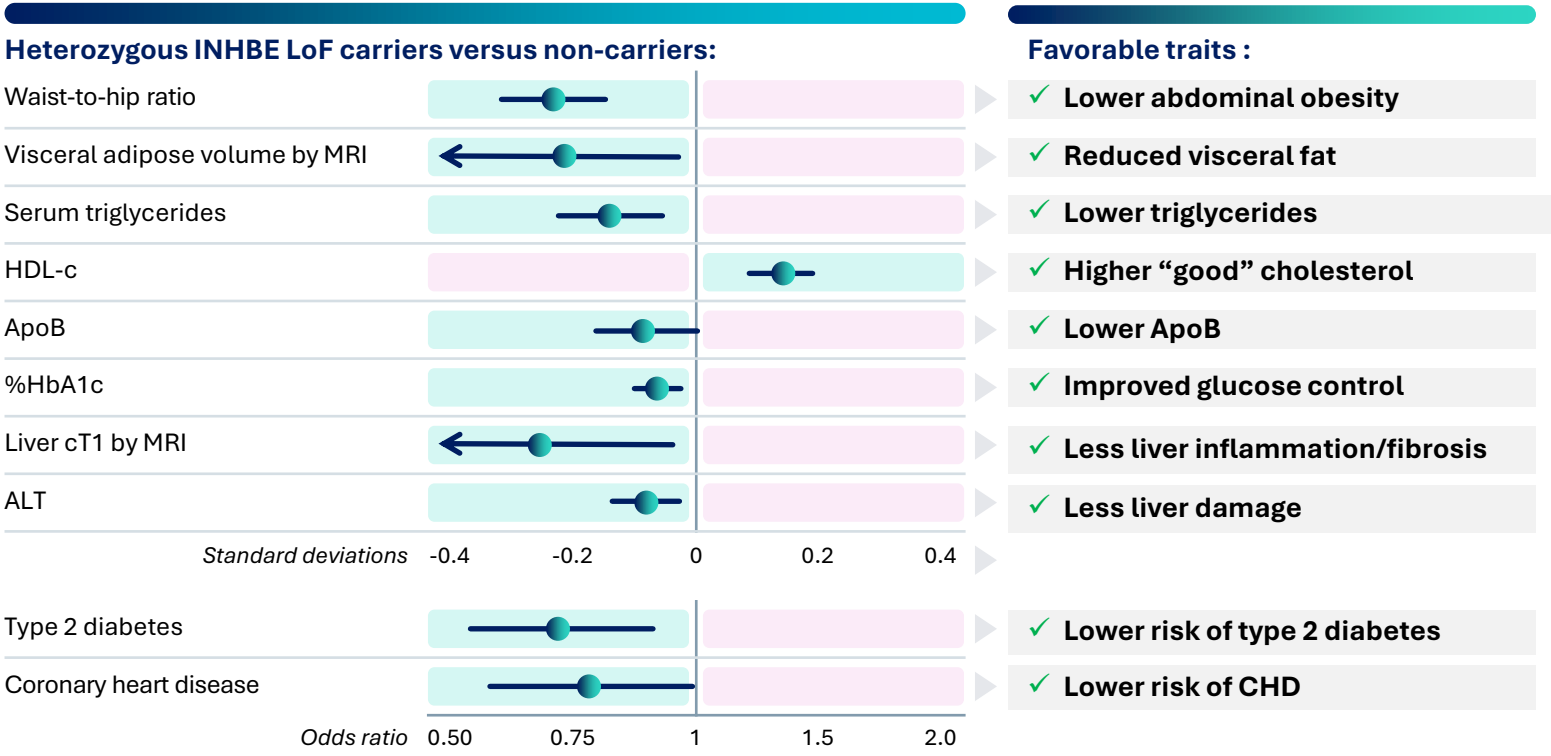
1. Sargeant, et al. 2019 *Endocrinol Metab* (Seoul) 34, 247; 2. Wegovy PI; 3. Ghusn and Hurtado. 2024 *Obesity Pillars* 12, 100127; 4. Leach, et al. 2023 *Prime Therapeutics Claims Analysis*; 5. Gasoyan, et al. 2024 *Obesity* (Silver Spring) 32, 486.

Human genetic data demonstrate that heterozygous INHBE loss-of-function (LoF) carriers have lower visceral fat and a healthier metabolic profile



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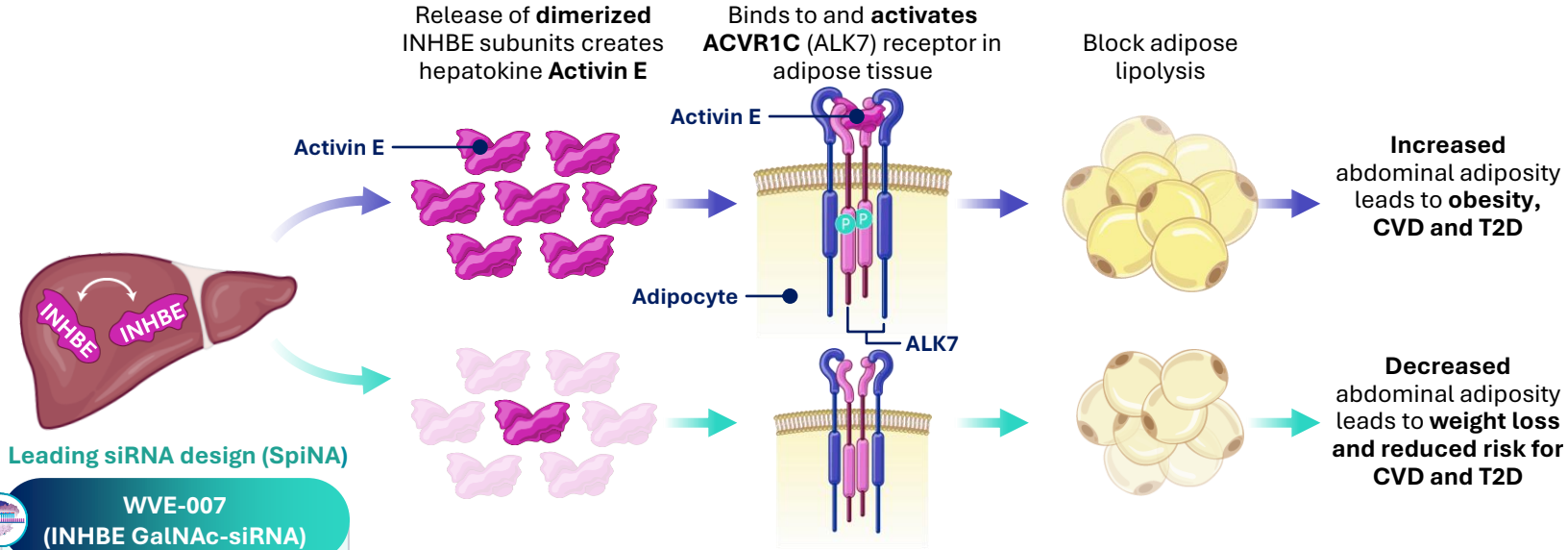
Akbari et al. *Nat Commun*. 2022 Aug 23;13(1):4844; Deaton et al. *Nat Commun*. 2022 Jul 27;13(1):4319. Waist-to-hip ratio, BMI-adjusted: Visceral adipose volume (MRI), BMI adjusted; HDL-c: high-density lipoprotein cholesterol; %HbA1c: glycated hemoglobin; ALT: alanine transaminase; ApoB: apolipoprotein B; CHD: coronary heart disease; cT1: corrected T1

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



Leading siRNA design (SpiNA)

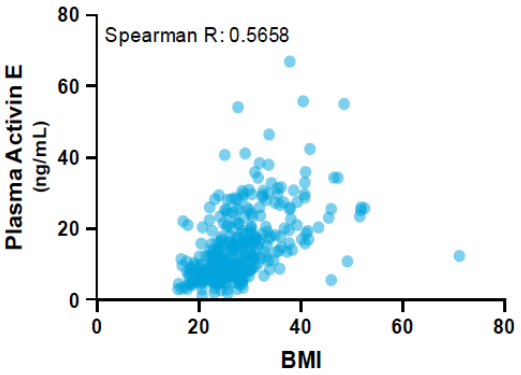
WVE-007 (INHBE GalNAc-siRNA)

- **Proprietary, clinically validated chemistry**
- **Potential for 1–2x yearly dosing**

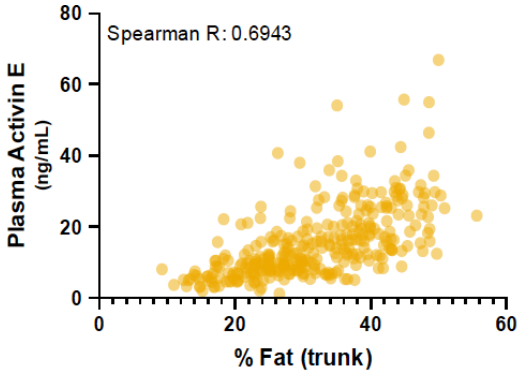
1. *Cell Reports* (2018) 25, 1193–1203; 2. *Biochemical Journal* (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8; SpiNA design is derived from Liu et al., 2023 Nucleic Acids Research doi: 10.1093/nar/gkad268.

Higher circulating Activin E levels are correlated with higher BMI, higher abdominal fat, and higher fasting insulin in non-diabetic adults

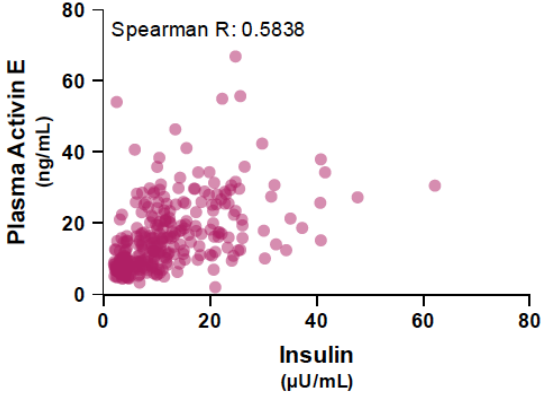
BMI



Abdominal Fat



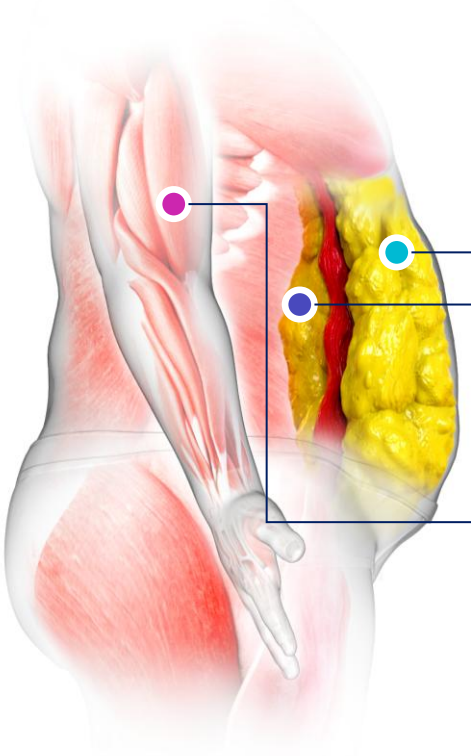
Fasting Insulin



Further supports INHBE suppression as a weight loss approach for individuals living with obesity

Dubey et al. Activin E levels correlate with indicators of metabolic dysfunction in humans. ObesityWeek 2025.

WVE-007 is designed to improve body composition by decreasing fat and preserving muscle



Subcutaneous fat

Visceral fat

Muscle

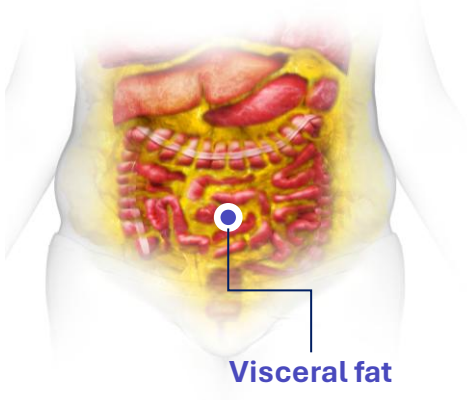
Total Fat REDUCED

Visceral Fat REDUCED

Muscle PRESERVED

WVE-007's mechanism is focused on lipolysis and directly reducing visceral and subcutaneous fat

Visceral fat drives insulin resistance and many cardiometabolic disorders



Waist circumference is a clinical proxy for visceral fat

- MASH
- Type 2 diabetes
- Cardiovascular diseases
- PCOS

Reduced visceral fat is associated with multiple health benefits

Visceral fat decrease

≥ 5%

Improved insulin sensitivity[1]: Lower HbA1c and better lipid profile

≥ 5-10%

Reduced cardiovascular risk[2]: Reduced blood pressure, improved lipids, lower systemic inflammation

≥ 10%

Reduced liver fat (steatosis)[3]: Significant reduction in hepatic triglycerides, improved liver enzymes

Decreased hepatic fibrosis[4]: Resolution of steatohepatitis in up to 90%, fibrosis regression in many cases

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

WVE-007 aims to address a key limitation of current standard of care: up to 40% of weight loss is driven by muscle loss

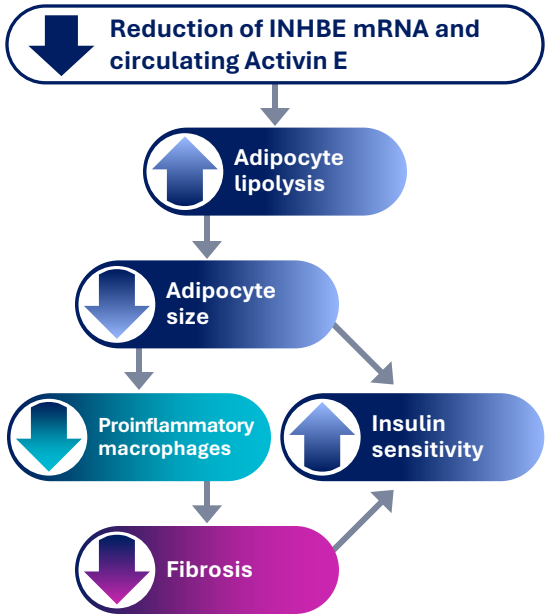
Preservation of muscle mass is linked to many health benefits

- Higher basal metabolic rate (BMR)[1]
- Improved insulin sensitivity[2,3]
- Increased caloric expenditure post-exercise[1]
- Preserve muscle strength and function[4]
- Reduced visceral fat[5,6]
- Prevent weight regain[7,8]
- Improved glucose homeostasis[2,3]
- Increased bone density, strength, function, and longevity[9,10]

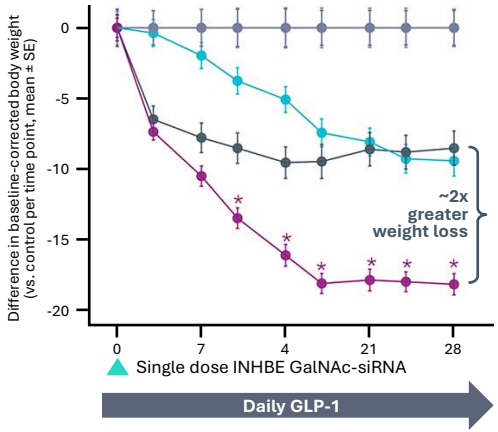
1. J. Clin. Med. 2024, 13, 5862; 2. J. Diab. Res. 2017, 8314852; 3. J. Funct. Morphol. Kinesiol. 2025, 10, 244; 4. J Bone Mineral Res. 2018, 33(2): 211–220; 5. Front. Nutr. 2023, 10:1246157; 6. Nat. Med. 2026, 32: 869–882; 7. Med Sci Sports Exerc. 2022, 54(12):2031-2036; 8. The Lancet eClinical Medicine, 2024, 69: 102475; 9. Ann Geriatr Med Res 2025, 29(1):1-14; 10. Age and Ageing, 2025, 54(7): afaf189; 11. Sargeant, et al. 2019 *Endocrinol Metab* (Seoul) 34, 247.

Preclinical data support WVE-007's potential to treat obesity and improve cardiometabolic health across treatment settings

Wave's INHBE GalNAc-siRNA drives fat reduction and improved insulin sensitivity

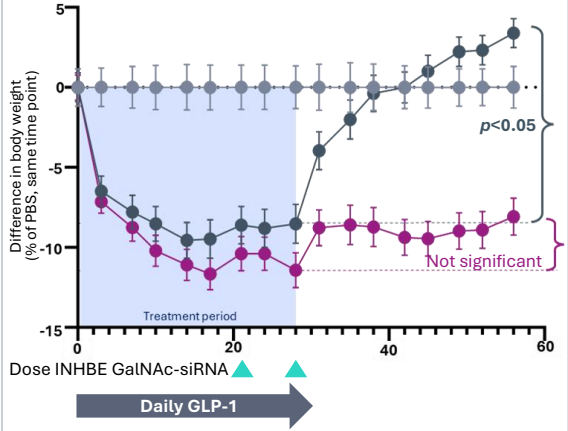


Weight loss similar to semaglutide in monotherapy; doubled when combined



Control for semaglutide
Control for siRNA
Semaglutide
INHBE GalNAc-siRNA
Semaglutide + INHBE GalNAc-siRNA

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



PBS
Semaglutide
Semaglutide + INHBE GalNAc-siRNA

Liu et al., 2023 Nucleic Acids Research doi: 10.1093/nar/gkad268; Data from preclinical studies conducted in mice fed with 60% high fat diet; Middle: semaglutide10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human. Middle 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.

INLIGHT clinical trial update

Christopher Wright, MD, PhD
Chief Medical Officer

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Today's update: Phase 1 (SAD) portion of INLIGHT 6-month data from 240 mg cohort and 3-month data from 400 mg cohort

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Phase 1 lower BMI (SAD)

- **BMI: 28–35 kg/m^2**
- **HbA1c: <5.9%**
- **Otherwise healthy**
- Assessments include: Safety and tolerability, PK, Activin E, body composition (DEXA), biomarkers, body weight
- No diet or exercise modifications

SAD Cohort 4
600 mg (n=32)

SAD Cohort 3
400 mg (n=32)

SAD Cohort 2
240 mg (n=32)

SAD Cohort 1
75 mg (n=8)
PK/PD and safety only (no DEXA)

Evaluate safety, tolerability, and PK

Phase 2a high BMI (MAD)

- **BMI: 35–50 kg/m^2**
- **HbA1c: up to 8%**

MAD high BMI+T2D cohorts

MAD high BMI cohorts

- Individuals with **higher BMI** and **comorbidities**
- Assessments to additionally include:
  - Body composition (MRI in addition to DEXA)
  - Liver fat (MRI-PDFF)
- Diet and exercise modifications included

Evaluate safety, tolerability, and PK; assess metabolic and body composition improvements as well as weight loss

SAD: single-ascending dose; MAD: multi-ascending dose; PK: pharmacokinetics.

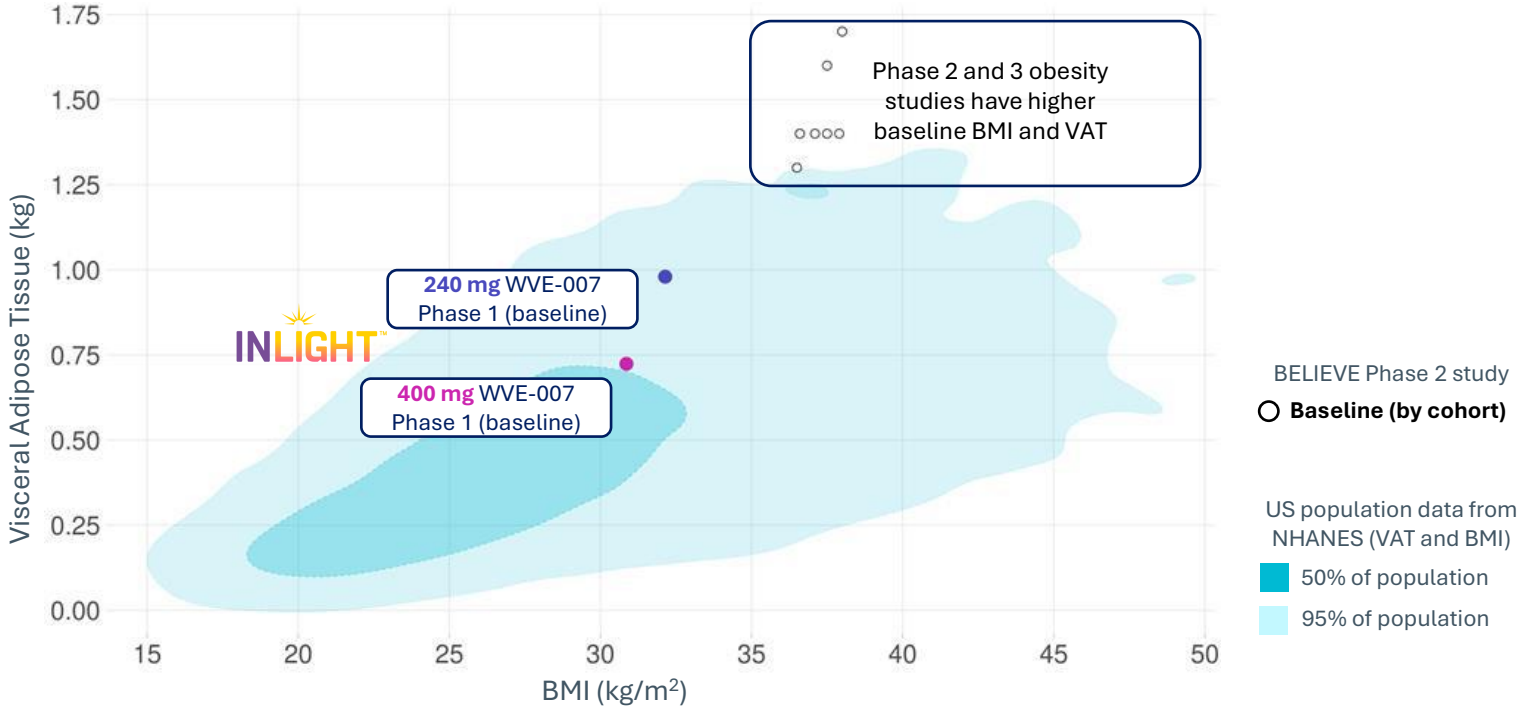
Baseline characteristics showed differences between 240 mg and 400 mg cohorts

400 mg cohort has lower baseline BMI, total and visceral fat with higher lean mass versus 240 mg cohort

INLIGHT Baseline Characteristics	Placebo N=18	WVE-007 75 mg N=6	WVE-007 240 mg N=24	WVE-007 400 mg N=24
Age at consent (years)	35.2 (8.8)	38.3 (3.7)	40.5 (11.2)	39.4 (9.4)
Gender,				
Male	10 (55.6)	2 (33.3)	15 (62.5)	17 (70.8)
Female	8 (44.4)	4 (66.7)	9 (37.5)	7 (29.2)
Weight (kg)	95.0 (12.5)	97.4 (15.5)	97.7 (17.0)	95.6 (11.4)
BMI (kg/m^2)	31.8 (2.4)	32.5 (2.8)	32.1 (2.9)	30.9 (1.7)
Waist circumference (cm)	103.2 (8.7)	105.0 (8.4)	106.4 (10.9)	105.2 (8.0)
Total fat mass (kg)	34.7 (5.4)	NA	34.2 (9.0)	33.5 (5.9)
Lean mass (kg)	57.5 (11.1)	NA	58.4 (10.8)	59.4 (10.5)
Visceral fat mass (kg)	0.9 (0.5)	NA	1.0 (0.6)	0.7 (0.5)

All values are mean (SD) or N (%). Total fat mass, lean mass and visceral fat mass were measured by DEXA in the 240 mg and 400 mg cohorts. Lean mass equals tissues excluding bone and fat. Visceral fat is measured in the android region. Placebo column includes participants randomized to placebo across three cohorts shown.

Participants in Phase 1 portion of INLIGHT have substantially lower baseline BMI and visceral fat than those in Phase 2 and 3 obesity studies



400 mg cohort has even lower baseline VAT and BMI compared to 240 mg cohort

NHANES population reference: Adults aged 20–59 with valid DXA-derived visceral adipose tissue measurements, pooled across 2011–2018 survey cycles (n = 11,934). VAT mass (kg) estimated from DXA (Hologic); BMI from measured height and weight. Contours represent 2D kernel density estimates of the cross-sectional population distribution. Clinical trial data overlaid as change from baseline within the NHANES VAT–BMI coordinate space. BELIEVE data points from Heymsfield SB, et al. 2026 *Nat Med* 32, 869–882.

WVE-007 continues to be generally safe and well tolerated

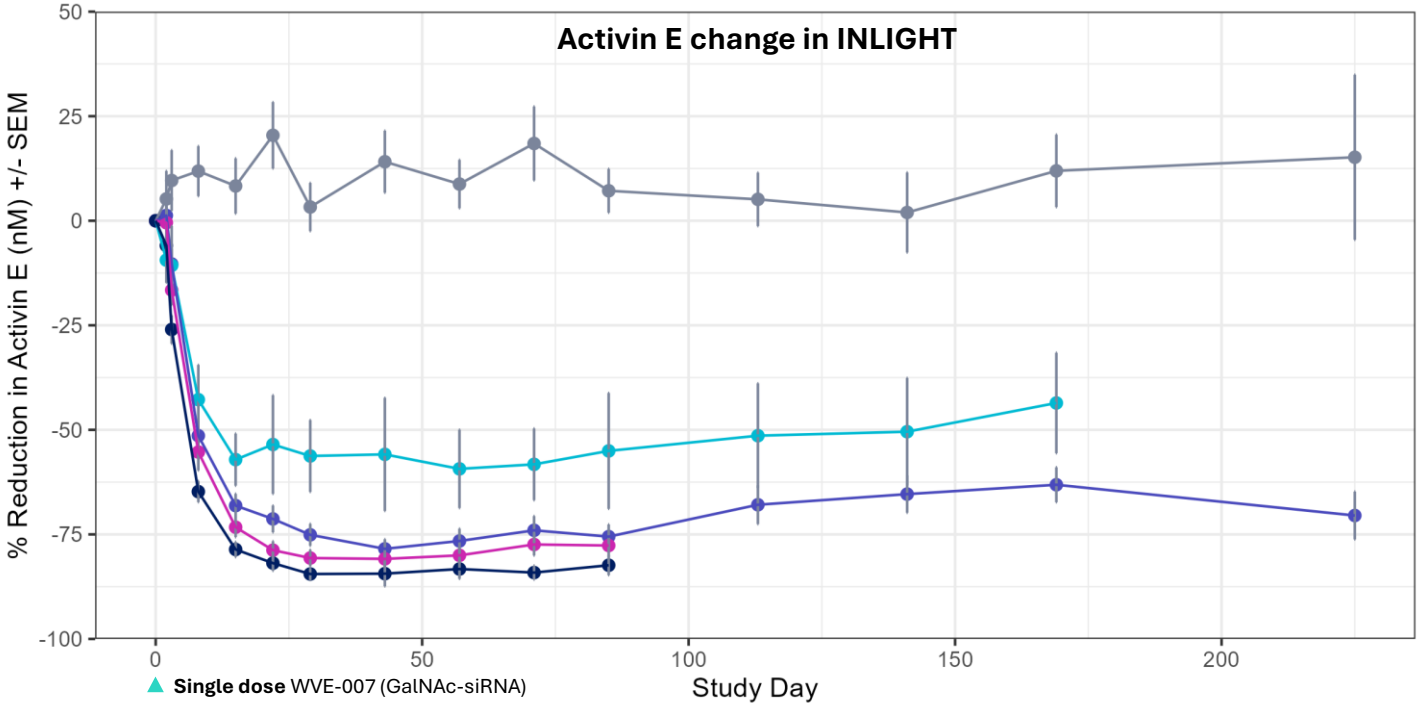
TEAE Category	Placebo N=26 n (%)	75 mg N=6 n (%)	240 mg N=24 n (%)	400 mg N=24 n (%)	600 mg N=24 n (%)
Any TEAE	19 (73.1)	3 (50.0)	20 (83.3)	17 (70.8)	15 (62.5)
Mild	9 (34.6)	2 (33.3)	13 (54.2)	9 (37.5)	9 (37.5)
Moderate	9 (34.6)	1 (16.7)	7 (29.2)	8 (33.3)	6 (25.0)
Severe	1 (3.8)	0	0	0	0
Any drug-related TEAE	3 (11.5)	1 (16.7)	9 (37.5)	9 (37.5)	10 (41.7)
Mild	3 (11.5)	1 (16.7)	9 (37.5)	9 (37.5)	10 (41.7)
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 treatment discontinuations, serious TEAEs, or deaths
- All TEAEs in the treatment group were mild or moderate
- All study drug 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 February 27, 2026; TEAE: treatment-emergent adverse event; LFT: liver function test
Placebo includes participants randomized to placebo across all cohorts.

Highly durable, dose dependent suppression of serum Activin E through at least seven months and mean max reductions of up to 88%



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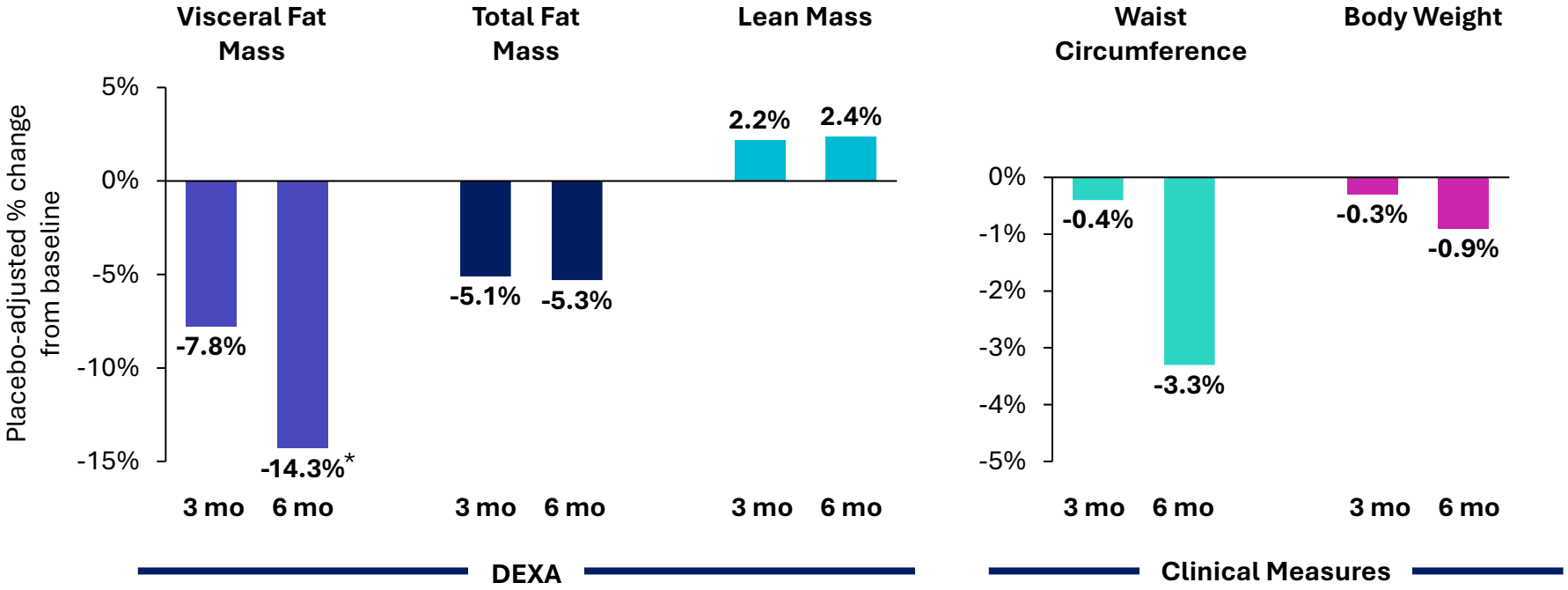
Dose
- Placebo (N=26)
- WVE-007 75 mg (N=6)
- WVE-007 240 mg (N=24)
- WVE-007 400 mg (N=24)
- WVE-007 600 mg (N=24)

Durability of suppression continues to support dosing WVE-007 once or twice per year

Figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. INLIGHT is ongoing, and Activin E data is still being collected in long-term follow-up for some timepoints and participant groups shown above.

Clinically meaningful improvements in body composition at six months following a single dose of WVE-007

WVE-007 (single dose 240 mg) at 3 months and 6 months



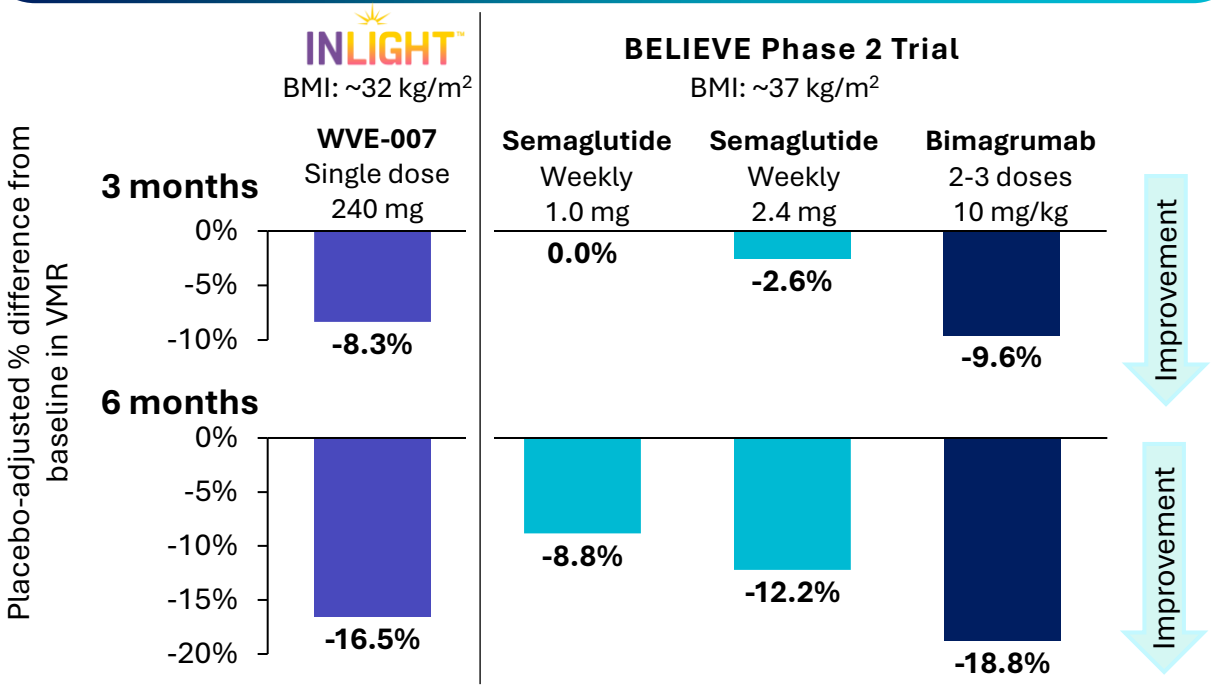
*p<0.05. Placebo-adjusted % change from baseline were estimated using an MMRM model with fixed effects for treatment group, visit, treatment-by-visit interaction, and baseline as a covariate; estimates were based on geometric mean ratios.

Single dose of WVE-007 in a lower BMI population led to greater improvement in body composition by VMR versus semaglutide

Visceral Fat-to-Muscle Ratio (VMR)

- Established measure of body composition integrating harmful visceral fat and beneficial lean mass in a single index
- Lower VMR is associated with decreased risk of MASH / MAFLD,[1,2] type 2 diabetes,[3] and cardiometabolic disorders (e.g., dyslipidemia, hypertension)[1,3]

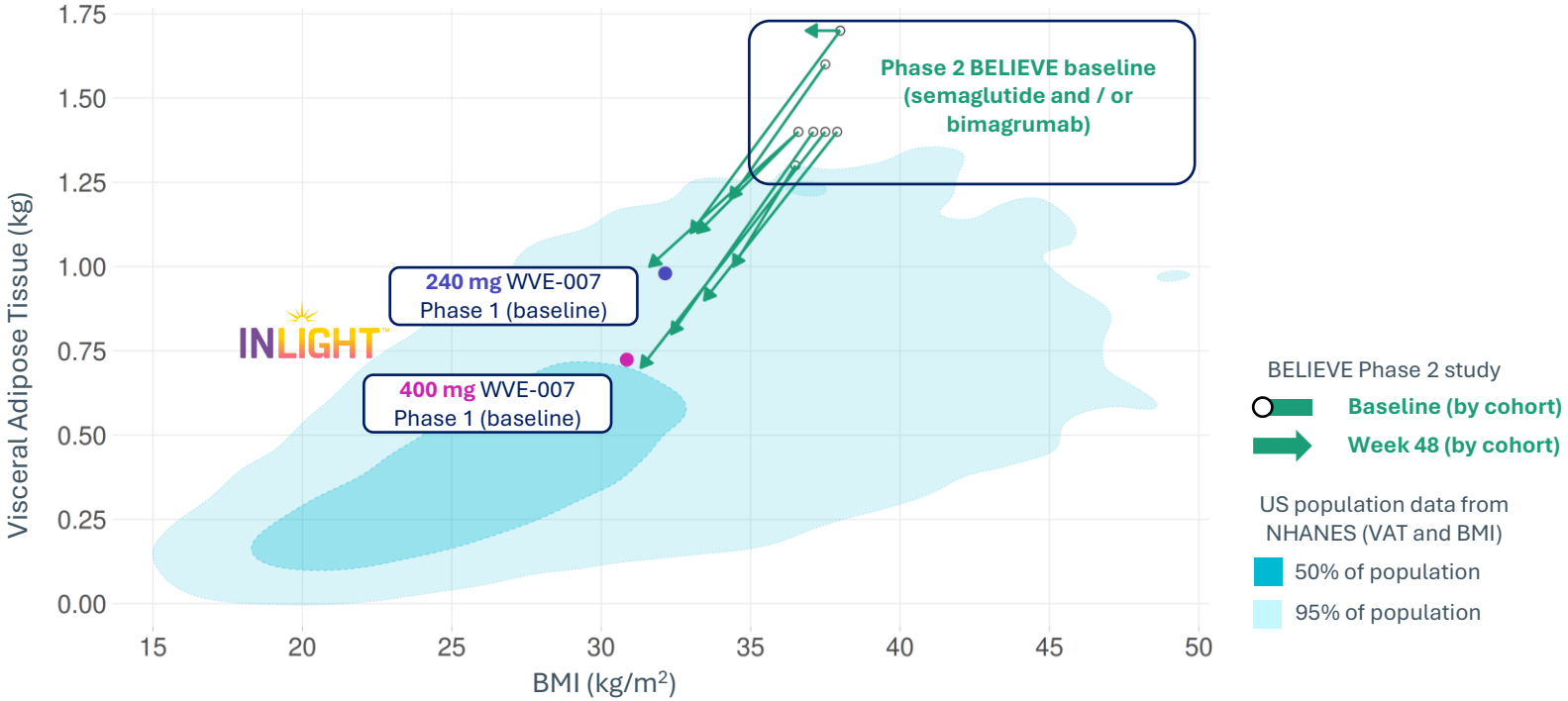
Improvement in body composition by VMR at 3 months and 6 months[4]



1. Zhang S, *et al.* 2023 *Diabetes Metab Res Rev.* 39(2):e3597; 2. Liu C, *et al.* 2024 *Lipids Health Dis.* 23(1):104; 3. Wang Q, *et al.* 2019 *Diabetes Metab Syndr Obes.* 12:1399-1407. 4. Placebo-corrected VMR calculated based on changes from baseline in visceral fat and lean mass at 3 and 6 mo. For BELIEVE, values are from Heymsfield SB, et al. 2026 *Nat Med* **32**, 869–882.

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.

INLIGHT Phase 1 participants start where those in the Phase 2 BELIEVE study end after treatment



400 mg cohort has even lower baseline VAT and BMI compared to 240 mg cohort

NHANES population reference: Adults aged 20–59 with valid DXA-derived visceral adipose tissue measurements, pooled across 2011–2018 survey cycles (n = 11,934). VAT mass (kg) estimated from DXA (Hologic); BMI from measured height and weight. Contours represent 2D kernel density estimates of the cross-sectional population distribution. Clinical trial data overlaid as change from baseline within the NHANES VAT–BMI coordinate space. BELIEVE data points from Heymsfield SB, et al. 2026 *Nat Med* 32, 869–882.

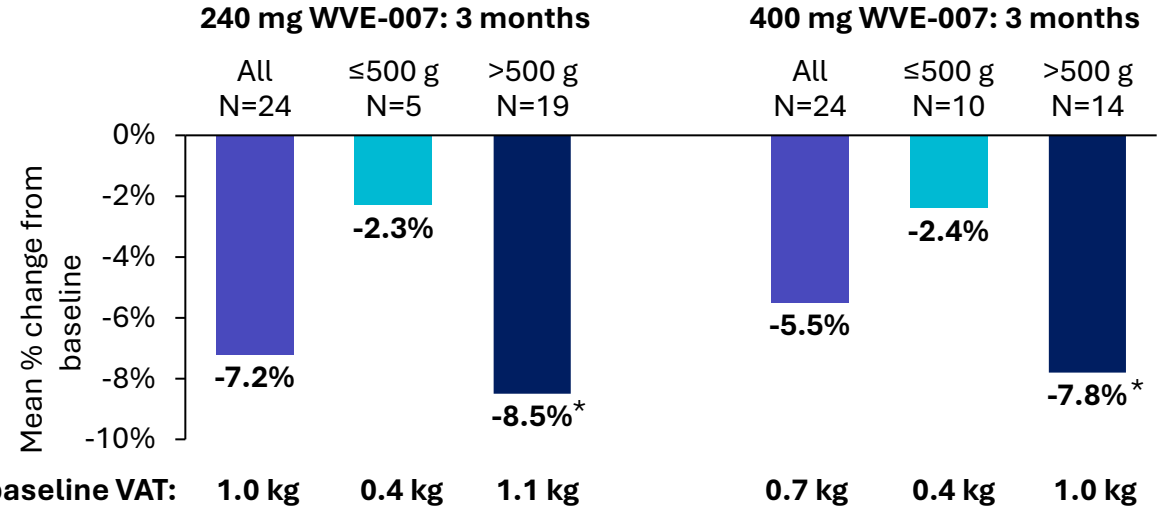
400 mg three-month results emphasize the impact of baseline body composition on therapeutic effect

Leaner baseline body composition, including lower BMI, and more participants with healthy levels of visceral fat (≤500 g)[1]

WVE-007 400 mg cohort
3-month results:

- Placebo-adj. changes from baseline in body composition following single dose
  - Visceral fat reductions (-5.0%)
  - Total fat reductions (-0.7%)
  - Lean mass preservation (-0.2%)
- 10 / 24 (42%) treated patients had healthy levels of visceral fat (≤500 g)
- Post-hoc analysis of 3-month results demonstrates more robust visceral fat reductions in individuals with higher baseline visceral fat (>500 g)

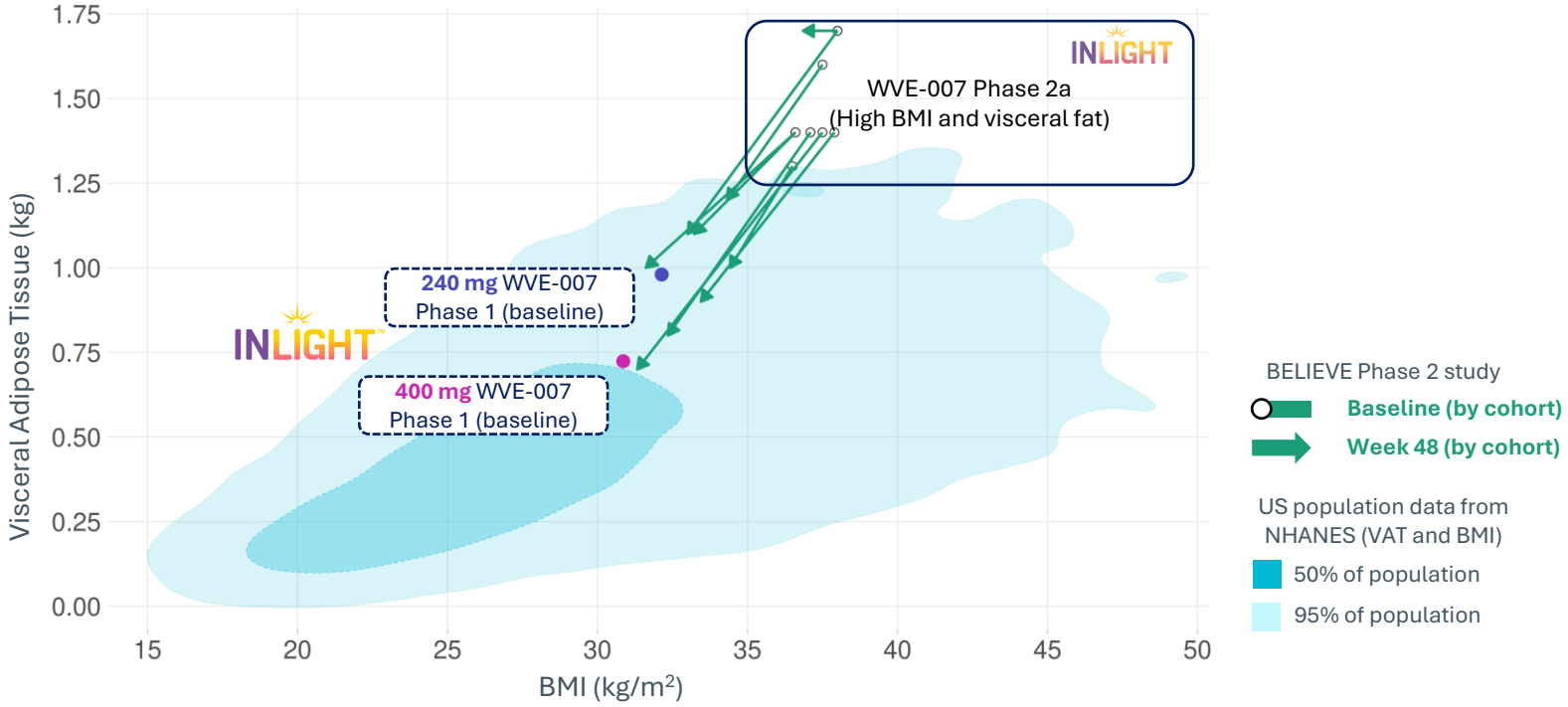
Post-hoc analysis: average visceral fat reductions by baseline VAT



Larger visceral fat reductions observed in participants with excess visceral fat and higher BMI at baseline

*p<0.05. Mean % CFB values are the arithmetic mean of individual % CFB and were tested within each subgroup against zero using a one-sample t-test.
Placebo-adjusted % CFB were estimated using an MMRM model with fixed effects for treatment, visit, treatment-by-visit interaction, and baseline as a covariate; estimates were based on geometric mean ratios. 1. Burridge K, et al. 2022 *Obes Pillars*.1:100007.

Phase 2a INLIGHT to evaluate higher BMI participants comparable to Phase 2 and Phase 3 obesity studies



Expect greater fat loss in INLIGHT Phase 2a with higher BMI and more excess fat

NHANES population reference: Adults aged 20–59 with valid DXA-derived visceral adipose tissue measurements, pooled across 2011–2018 survey cycles (n = 11,934). VAT mass (kg) estimated from DXA (Hologic); BMI from measured height and weight. Contours represent 2D kernel density estimates of the cross-sectional population distribution. Clinical trial data overlaid as change from baseline within the NHANES VAT–BMI coordinate space. BELIEVE data points from Heymsfield SB, et al. 2026 *Nat Med* 32, 869–882.

High BMI Phase 2a (MAD) global, placebo-controlled study will inform further development in obesity, as well as MASH, type 2 diabetes, and CVD

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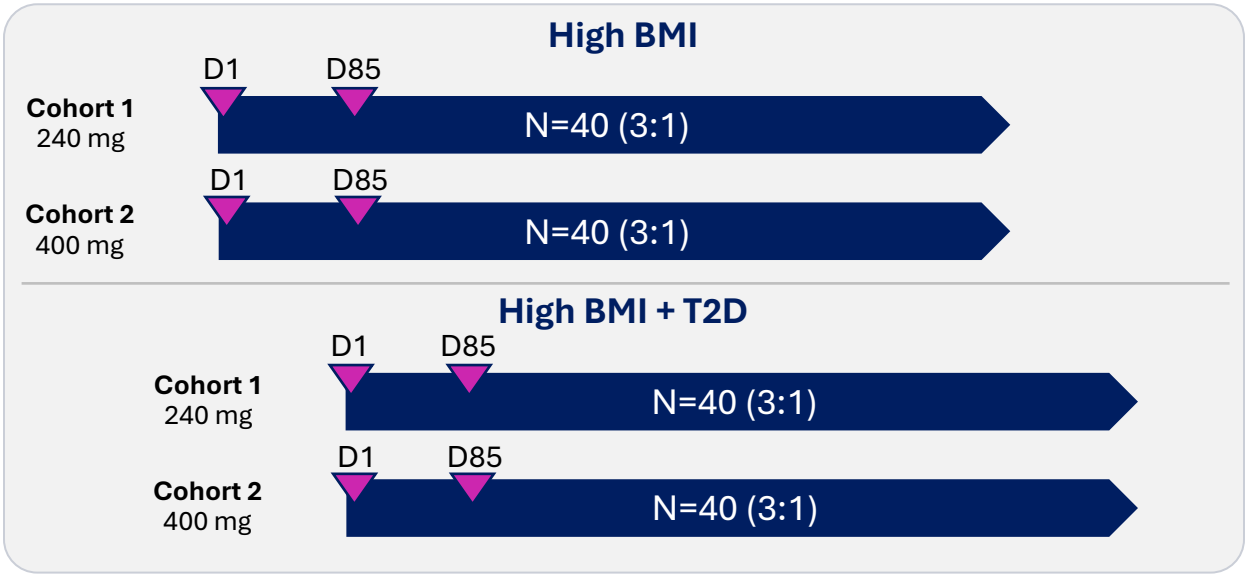


- Individuals with **higher BMI** (35–50 kg/m^2) and **comorbidities**
- Assessments include:
  - Body weight
  - Body composition (MRI in addition to DEXA)
  - Liver fat (MRI-PDFF)
  - HbA1c, lipid levels, CRP
  - Muscle function
- Diet and exercise modifications included
- 12-month study duration
  - First assessment Day 85 (3 months)

Expect to initiate high BMI Phase 2a (MAD) portion of INLIGHT in 2Q 2026

SAD: single-ascending dose; MAD: multi-ascending dose; PK: pharmacokinetics; MASH: metabolic dysfunction-associated steatohepatitis; CVD: cardiovascular disease

On track to initiate multiple trials of WVE-007, including as an incretin add-on and as post-incretin maintenance in 2026

Monotherapy

Single agent in individuals living with obesity

INLIGHT™

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

Add-on

Combination with incretin treatments

- To leverage an orthogonal mechanism to incretins for enhanced efficacy

Maintenance

An off-ramp post-incretin treatments

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

Potential to address more than one billion individuals with obesity globally

Phelps, NH, et al. 2024 Lancet 403, 1027

Opportunity for WVE-007 and next steps

Paul Bolno, MD, MBA

President and CEO

WAVE LIFE SCIENCES

Opportunity to deliver a transformative obesity therapeutic profile

WVE-007

- Drives meaningful improvements in body composition:
  - Visceral fat loss
  - Reduction in waist circumference
  - Total fat loss
  - Muscle preservation
  - Reduction in body weight
- Potential 1–2x per year dosing
- Generally safe and well tolerated

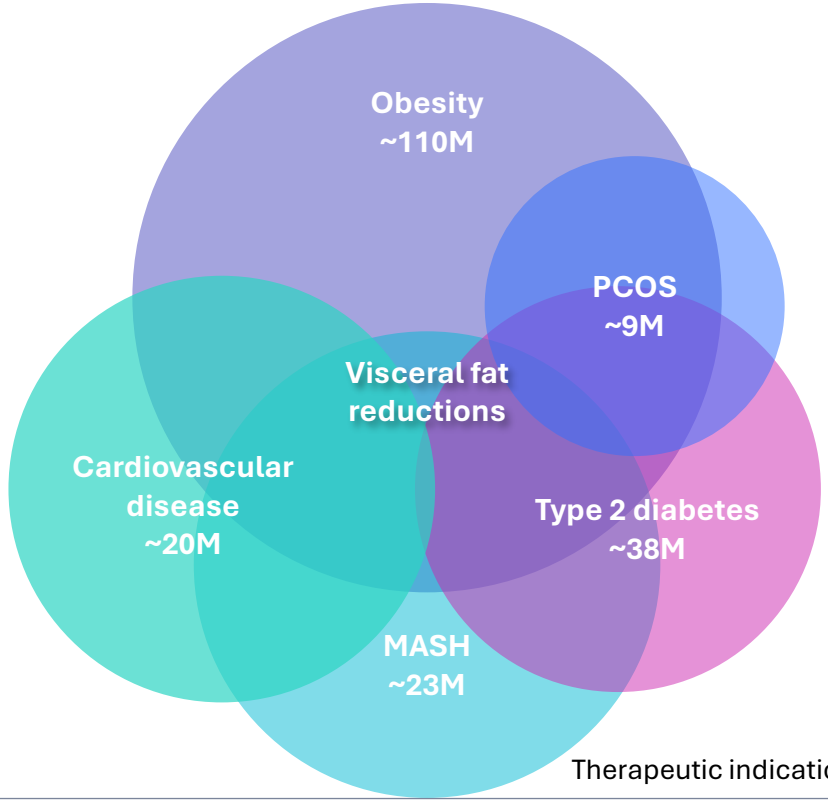
Next stages of development

- High BMI Phase 2a (MAD) study
- WVE-007 as an incretin add-on and as post-incretin maintenance

Opportunities to measure

- Further improvements in body composition
- >5% weight loss driven entirely off fat; muscle preservation
- Efficacy as add-on and maintenance
- Improvement of risk factors

INHBE silencing provides opportunity to address additional significant indications through lowering of visceral fat



Therapeutic indications and US patient populations

PCOS, polycystic ovary syndrome

1. All prevalence are US estimates. Prevalence of obesity, type 2 diabetes, and cardiovascular disease based on CDC / NHANES figures. MASH prevalence estimated from Estes, C. et al. 2018 Hepatology 67, 123. PCOS prevalence based on WHO estimates.

Anticipated 2026 milestones for WVE-007 and WVE-006

WVE-007
(INHBE)
Obesity

2Q 2026
- **Initiate Phase 2a multidose** portion of INLIGHT in individuals with **higher BMI** and **comorbidities**

INLIGHT

2026
- **Additional data** from INLIGHT, including data from the **600 mg** Phase 1 SAD **cohort**

INLIGHT

2026
- **Initiate** new clinical trials evaluating WVE-007 as an **incretin add-on** and as **post-incretin maintenance**

WVE-006
(SERPINA1)
AATD

2Q 2026
- **Deliver data** from the **400 mg** multidose cohort and **600 mg** single dose cohort of RestorAATion-2 at the **ATS conference in May**

RESTORAATION

Mid-2026
- Receive **regulatory feedback** on a potential **accelerated approval pathway**

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

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For questions contact:
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