Wave Life Sciences

Corporate Presentation

April 28, 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.

WAVE® LIFE SCIENCES

Our Mission

To unlock the broad potential of RNA medicines to transform human health

Building a leading RNA medicines company

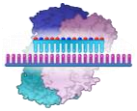
Differentiated RNA medicines platform and chemistry

PRISM

- **Proprietary chemistry**
- Leveraging deep insights in **human genetics**
- Strong and **broad IP**
- **In-house GMP** manufacturing

Translating genetic insights into potentially best-in-class medicines

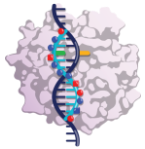
RNAi



WVE-007 (obesity)

- Differentiated mechanism focused on fat loss and muscle preservation

RNA editing



WVE-006 (AATD)
WVE-008 (liver disease)

- Restoration of functional protein production

Other modalities: **Splicing, antisense silencing**

Unlocking emerging pipeline

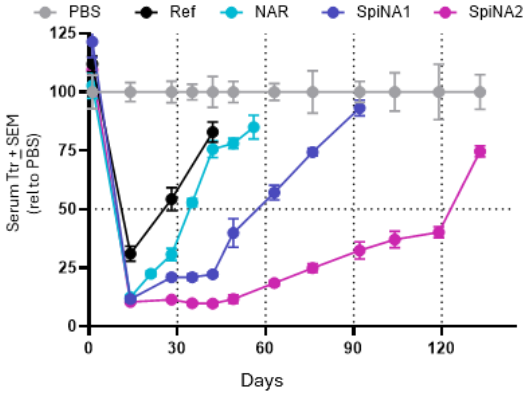
- **Extra-hepatic capabilities:** with RNAi and RNA editing
- **Bifunctional modalities:** single oligonucleotide constructs for dual RNAi silencing or RNAi silencing + RNA editing

Well capitalized with expected cash runway into 3Q 2028

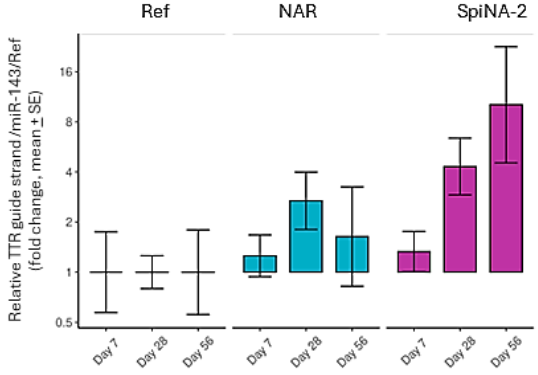
For over a decade Wave has been extending the frontiers of RNA therapies delivering breakthroughs in nucleic acid chemistry

RNAi — SpiNA

Protein reduction

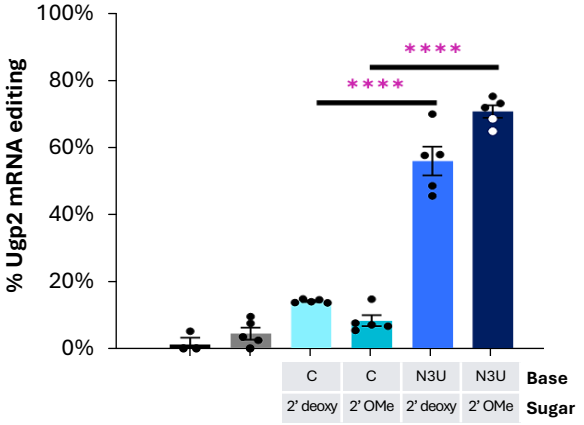


Ago2 loading



Substantial improvements in potency, duration of activity, and Ago2 loading with Wave's proprietary SpiNA design

RNA editing — AIMer



Increased RNA editing efficiency achieved with proprietary chemistry

Proprietary chemistry has dramatically increased potency and durability

Robust RNA medicines pipeline with first-in-class RNAi and RNA editing programs

Program	Discovery	IND / CTA Enabling Studies	Clinical	Patient population (US & Europe)
RNAi (SpiNA)				
WVE-007 (GalNAc) INHBE (obesity)				**175M** **(>1 billion globally)**
GalNAc / extra-hepatic Multiple				--
RNA EDITING (AIMer)				
WVE-006 (GalNAc) SERPINA1 (AATD)				**200K**
WVE-008 (GalNAc) PNPLA3 (liver disease)				**9M**
GalNAc / extra-hepatic Multiple				--
SPLICING				
WVE-N531 Exon 53 (DMD)				**2.3K**
Other exons (DMD)				**Up to 18K**
ALLELE-SELECTIVE SILENCING				
WVE-003 mHTT (HD)				**25K Symptomatic (SNP3)** **60K Pre-Symptomatic (SNP3)**

AATD: Alpha-1 antitrypsin deficiency; DMD: Duchenne muscular dystrophy; HD: Huntington's disease

WVE-007
GalNAc-siRNA silencing

Obesity

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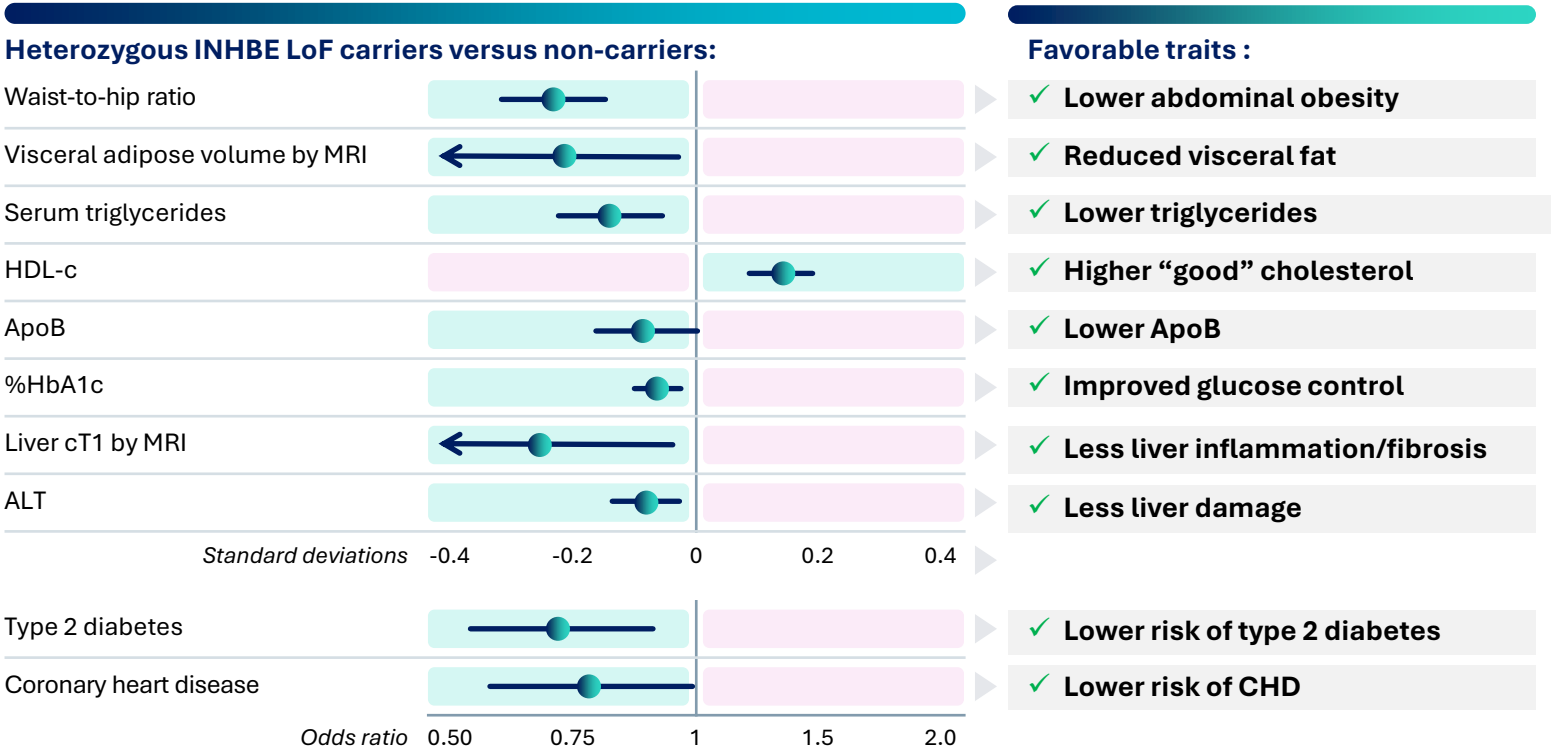
1. Sargeant, et al. 2019 *Endocrinol Metab* (Seoul) 34, 247; 2. Wegovy PI; 3. Ghusn and Hurtado. 2024 *Obesity Pillars* 12, 100127; 4. Leach, et al. 2023 *Prime Therapeutics Claims Analysis*; 5. Gasoyan, et al. 2024 *Obesity* (Silver Spring) 32, 486.

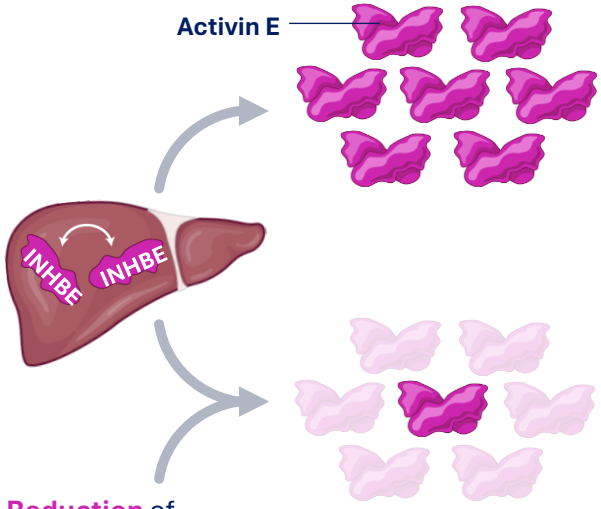
Human genetic data demonstrate that heterozygous INHBE loss-of-function (LoF) carriers have lower visceral fat and a healthier metabolic profile



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 has the potential to treat obesity and associated metabolic diseases

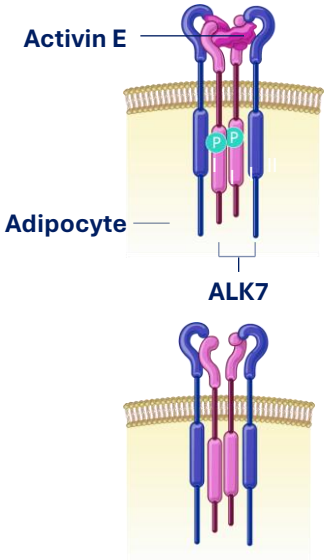
Release of **dimerized** INHBE subunits creates hepatokine **Activin E**



Reduction of INHBE mRNA with GalNAc-siRNA

Reduced release of hepatokine **Activin E**

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



Diminished activation of **ACVR1C** (ALK7) receptor in adipose tissue

Block adipose lipolysis

Increased adipose lipolysis and shrink adipocytes

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

Decreased abdominal adiposity leads to **weight loss and reduced risk for CVD and T2D**

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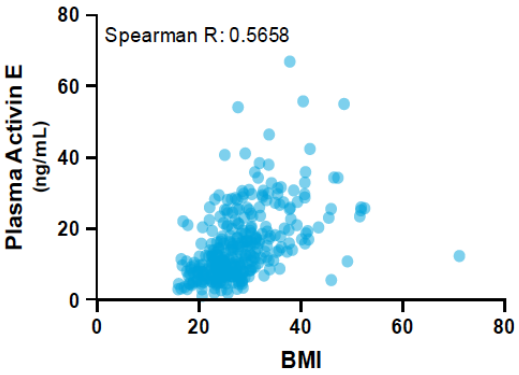
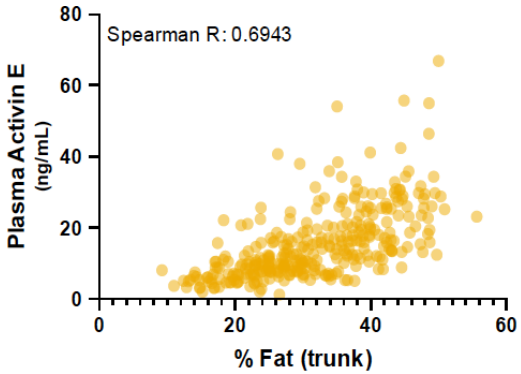
1. Cell Reports (2018) 25, 1193–1203; 2. Biochemical Journal (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8

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

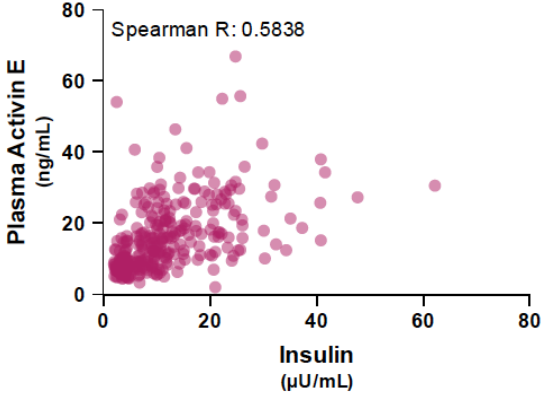
BMI



Abdominal Fat



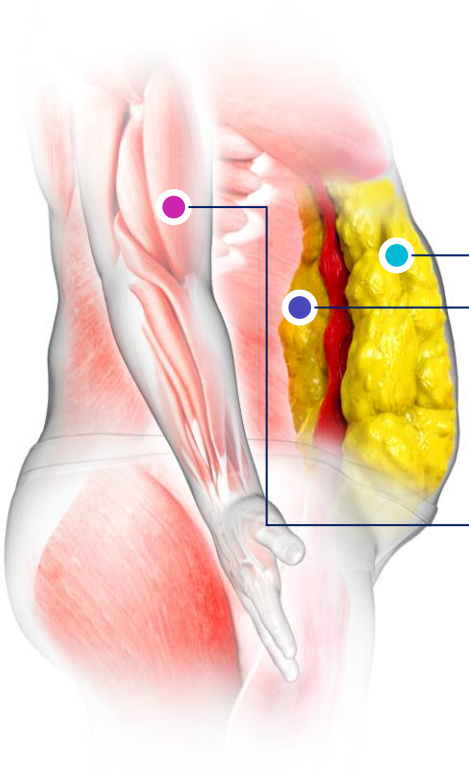
Fasting Insulin



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

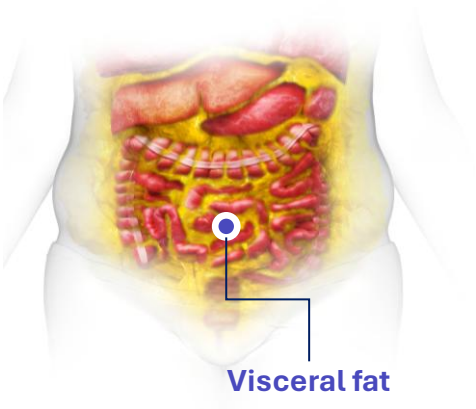
Total Fat REDUCED

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

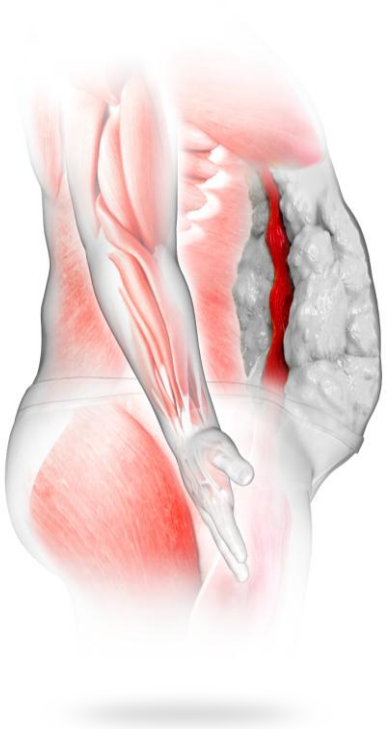
≥ 10%

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

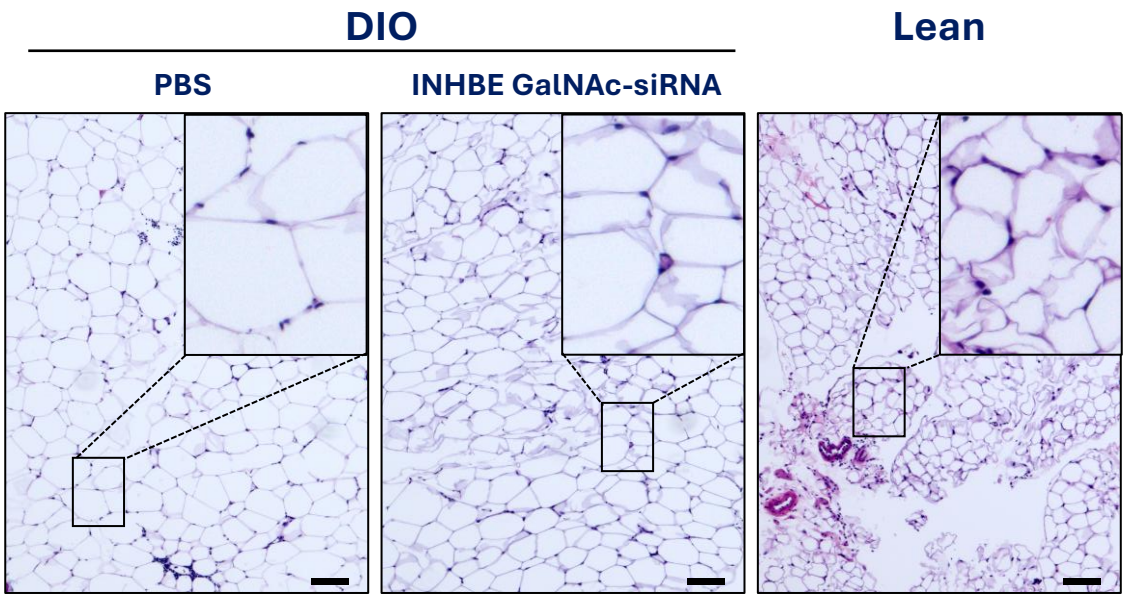


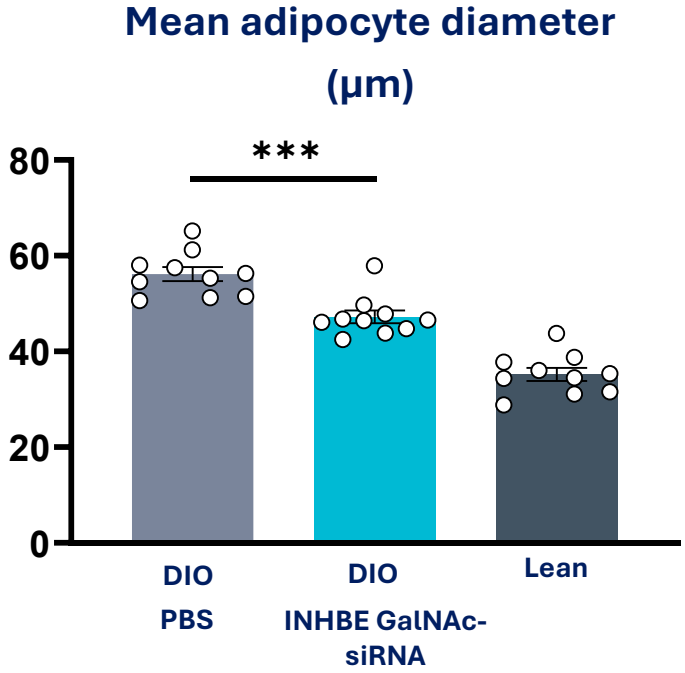
Preservation of muscle mass is linked to many health benefits

- 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.

A single dose of INHBE GalNAc-siRNA led to shrinkage of adipocytes in DIO mice

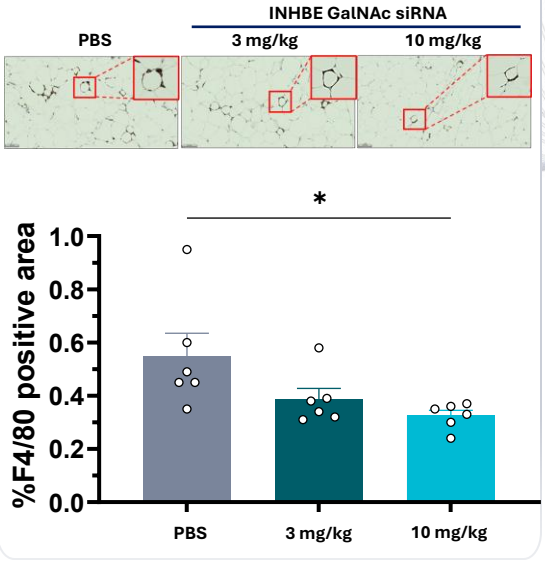




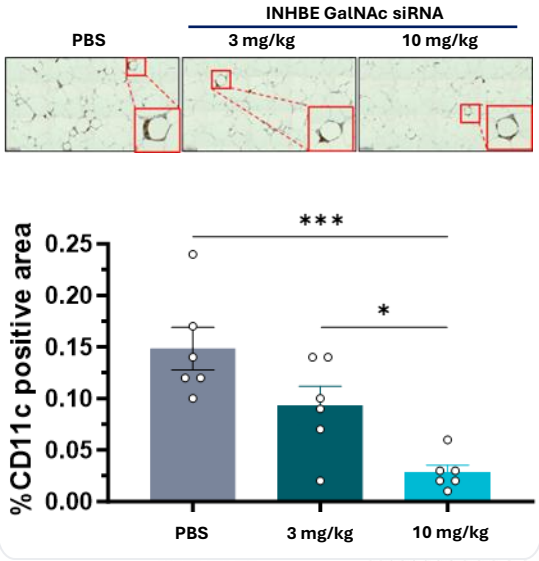
Data presented at ADA Scientific Sessions June 2025
***p<0.001; Day 28

A single dose of INHBE siRNA led to a lower inflammatory state of visceral adipose tissues in DIO mice, with strong suppression of pro-inflammatory M1 macrophages in visceral fat

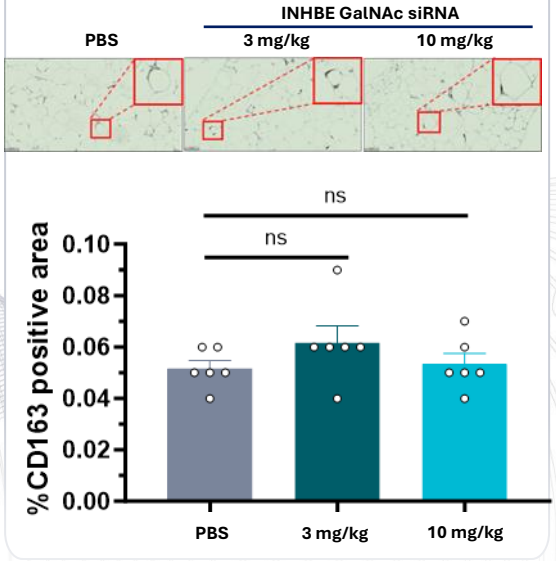
Macrophages (Mϕ) (F4/80)



Pro-inflammatory (M1) Mϕ (CD11c)



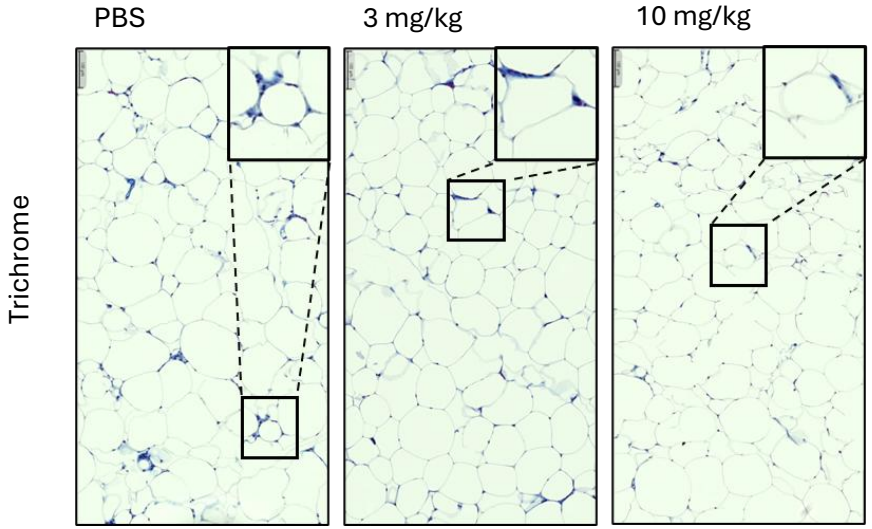
Anti-inflammatory (M2) Mϕ (CD163)



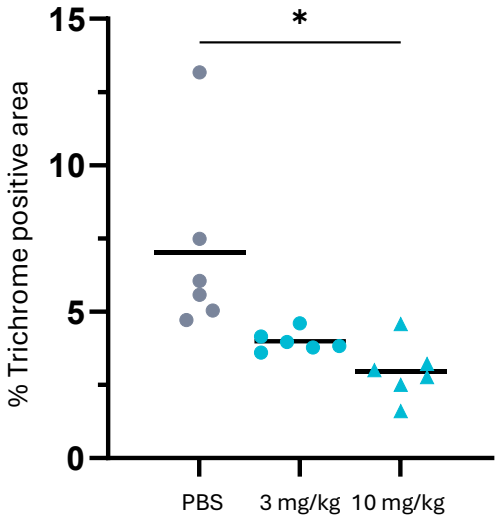
Data presented at ADA Scientific Sessions June 2025
***p<0.001, *p<0.05, ns=non-significant

Lowering of inflammatory state of epiWAT visceral fat induced by single dose of INHBE siRNA resulted in 58% reduction of adipose fibrosis

Reduced staining illustrates decreased tissue fibrosis



Fibrosis in mouse adipose (Day 56)



Data are means ± SEM of 6 mice. Each dot represents an individual mouse. Kruska-Wallis test with Dunn's multiple comparisons. *P<0.05

Treatment with WVE-007 (investigational INHBE 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 delivery (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
- ↓ Fibrosis
- ↑ Insulin sensitivity

And improving clinical outcomes

Cardiometabolic outcomes

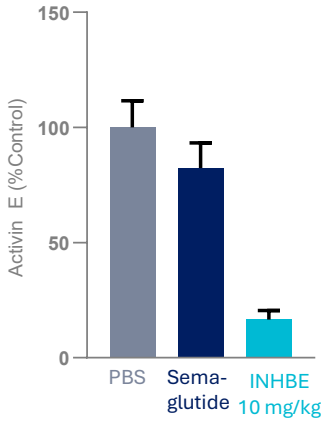
- ↓ Risk of CVD
- ↓ Risk of T2D

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

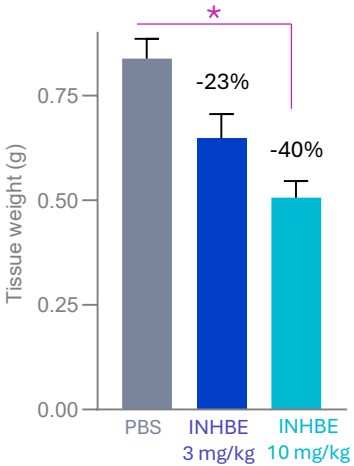
Durable Activin E reduction

Serum Activin E



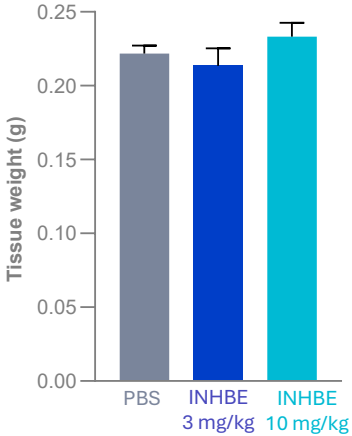
Reduction in fat

Epididymal fat weight



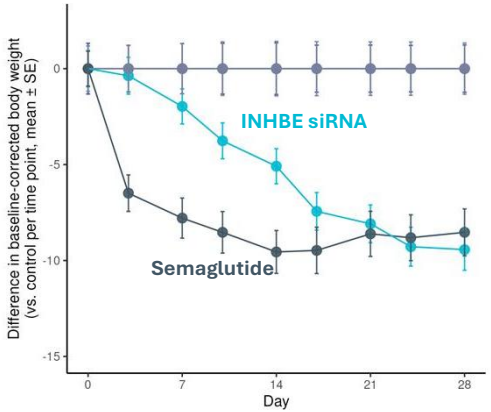
Muscle preservation

Quadricep weight



Reduction in body weight

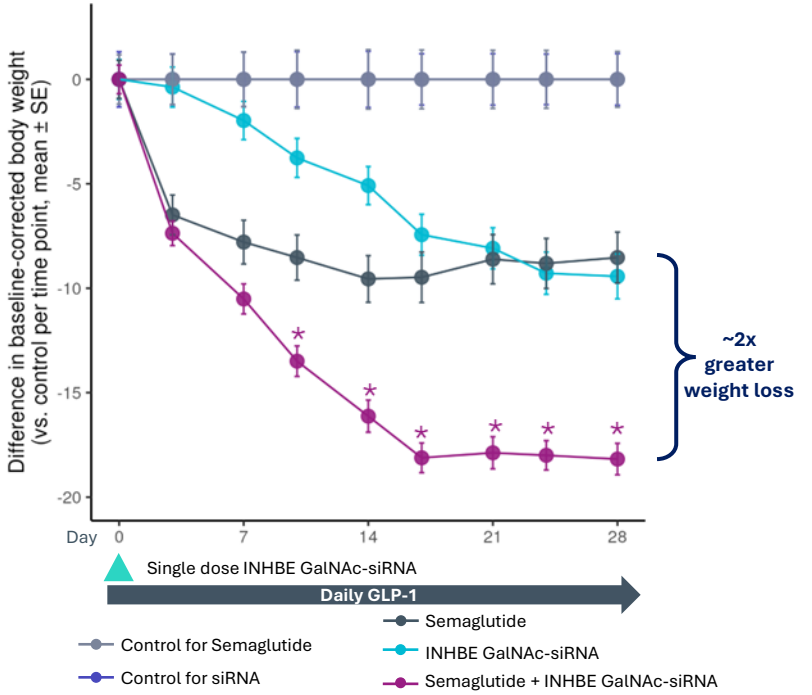
Single dose INHBE GalNAc-siRNA



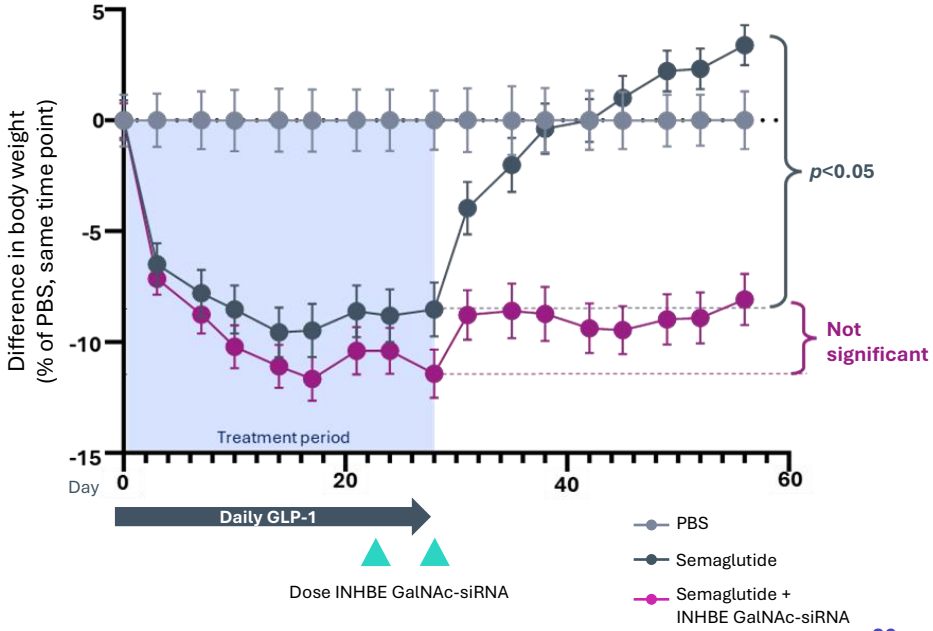
Left and right panels: Semaglutide 10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human; INHBE GalNAc-siRNA 10 mg/kg dose. All data from preclinical studies were conducted in mice fed with 60% high fat diet. Linear Mixed Effects ANOVA with post hoc comparisons of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

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 regain



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

Phase 1 portion of INLIGHT trial is investigating WVE-007 in individuals living with overweight or obesity, otherwise healthy

INLIGHT™

Phase 1 lower BMI (SAD)

- **Average BMI: 32 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)

MAD high BMI (35–50 kg/m^2)+T2D cohorts

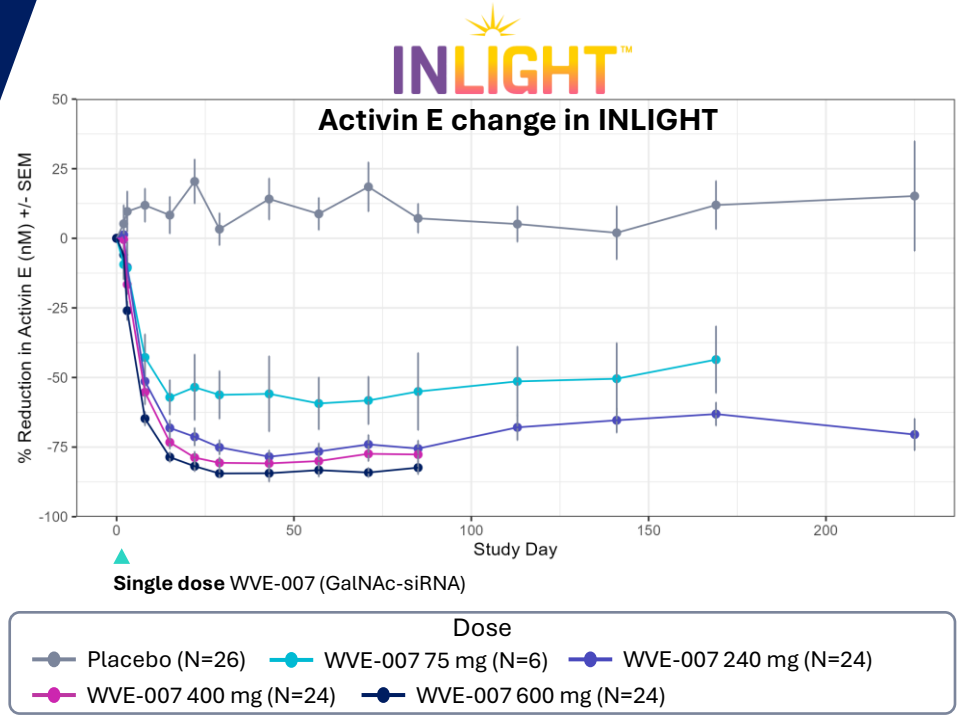
MAD high BMI (35–50 kg/m^2) cohorts

- Individuals with **higher BMI with and without type 2 diabetes**
- 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. Average BMI of 75 mg, 240 mg, and 400 mg cohorts.

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



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**

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

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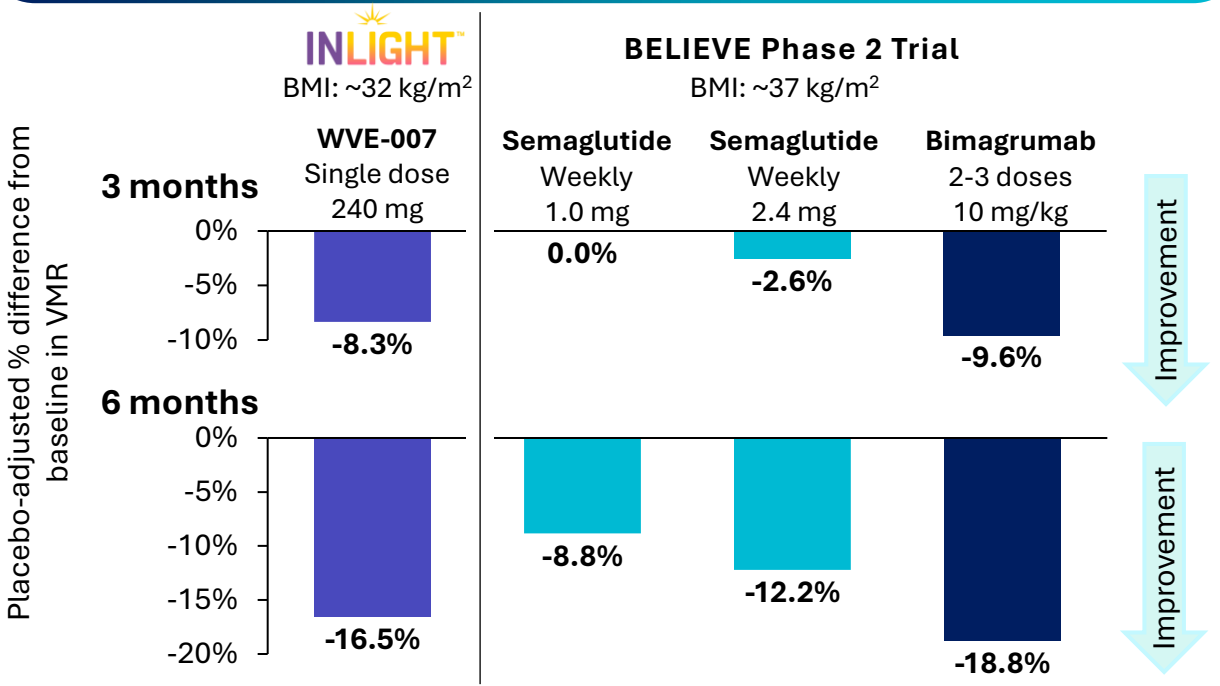
INLIGHT interim Phase 1 data reported March 26, 2026; Left: figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. Right: *p<0.05. All reductions are placebo-adjusted % change from baseline were estimated using an MMRM model with fixed effects for treatment group, visit, treatment-by-visit interaction, and baseline as a covariate; estimates were based on geometric mean ratios.

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]

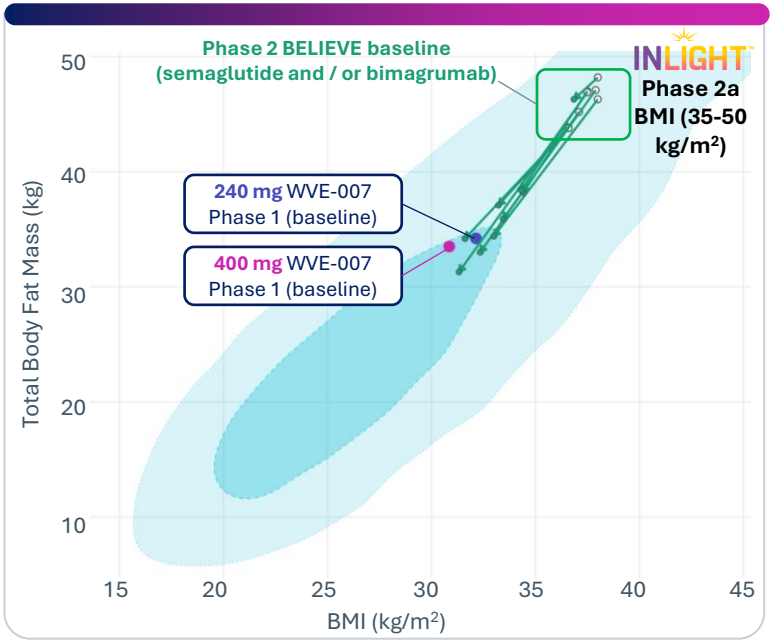


1. Zhang S, *et al.* 2023 *Diabetes Metab Res Rev.* 39(2):e3597; 2. Liu C, *et al.* 2024 *Lipids Health Dis.* 23(1):104; 3. Wang Q, *et al.* 2019 *Diabetes Metab Syndr Obes.* 12:1399-1407. 4. Placebo-corrected VMR calculated based on changes from baseline in visceral fat and lean mass at 3 and 6 mo.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

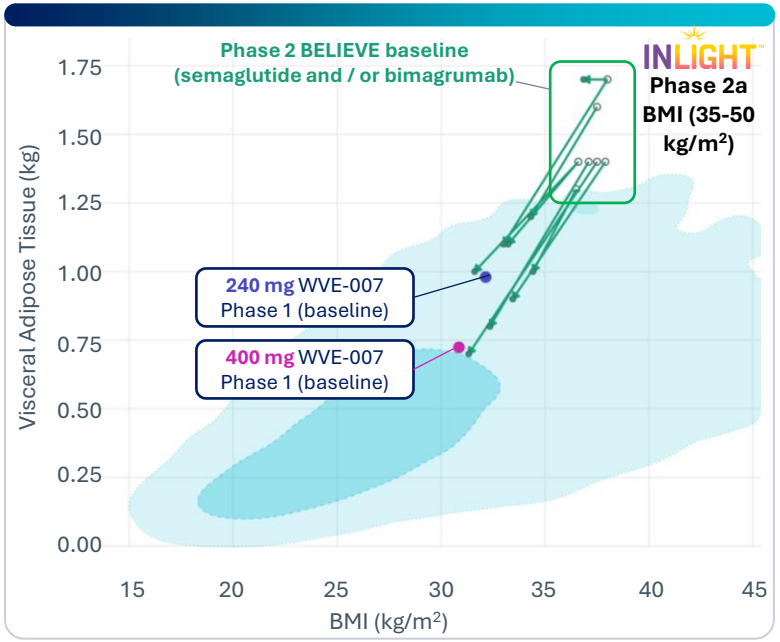
Note: The data presented above are derived from different clinical trials with differences in trial design and patient population, including with respect to BMI. As a result, cross-trial comparisons cannot be made and no head-to-head clinical trials have been conducted.

INLIGHT Phase 2a: higher BMI population aligns with Phase 2 and 3 obesity trials, potential for continued improvements in body composition

Total fat and BMI at baseline



Visceral fat and BMI at baseline



BELIEVE Phase 2 study

- Baseline (by cohort)
- Week 48 (by cohort)

US population data from NHANES (VAT and BMI)

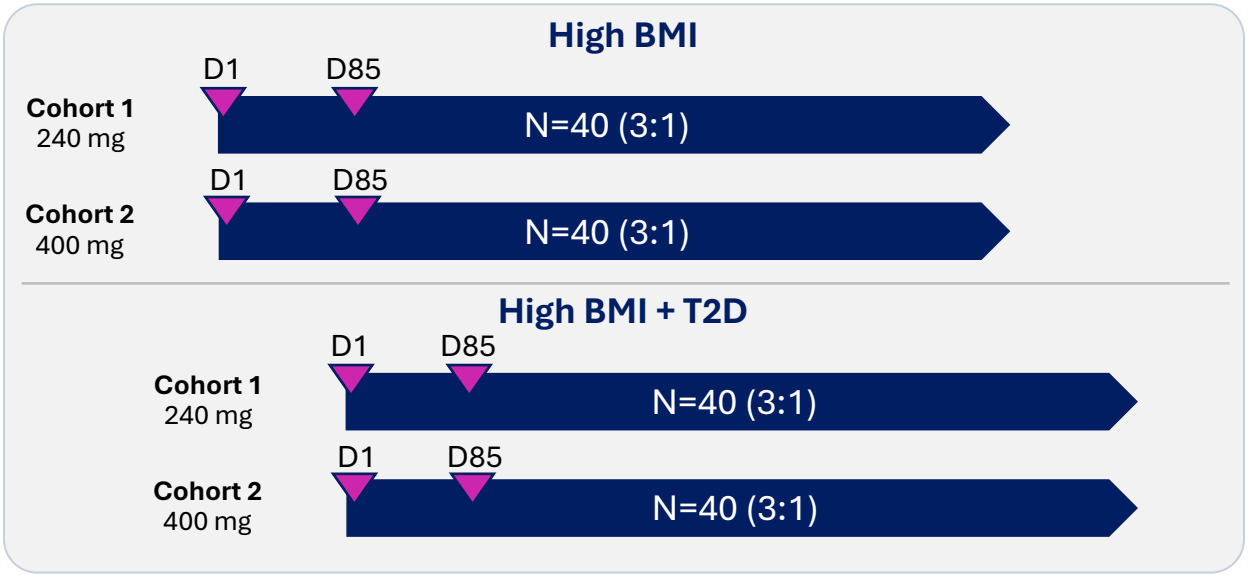
- 50% of population
- 95% of population

Expect greater fat loss in INLIGHT Phase 2a in participants with 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

INLIGHT™



- 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 the Phase 2a portion of INLIGHT in 2Q 2026; combination and maintenance studies of WVE-007 expected to initiate in 2026

Monotherapy

Single agent in individuals living with obesity

INLIGHT™

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

Combination

Add-on to incretin treatments

- To leverage an orthogonal mechanism to incretins for enhanced efficacy

Maintenance

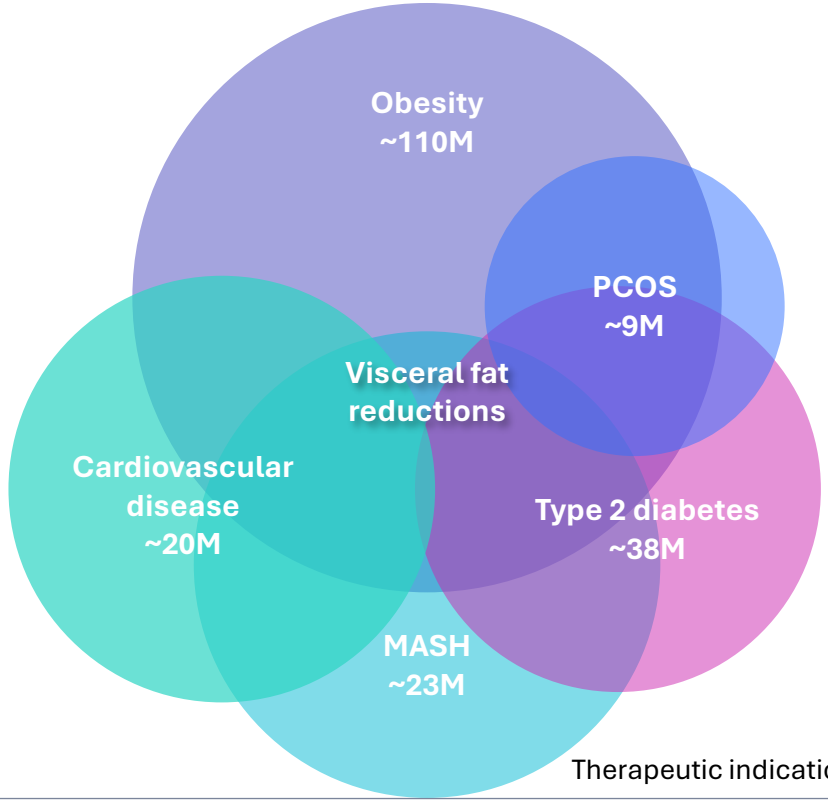
An off-ramp post-incretin treatments

- To prevent weight 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

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.

WVE-006
RNA editing (AIMer)

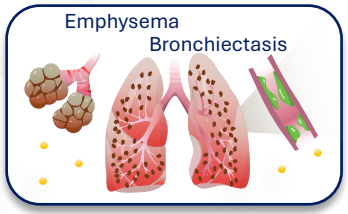
Alpha-1 antitrypsin deficiency (AATD)

WAVE LIFE SCIENCES

AATD impacts multiple organ systems and has limited treatment options

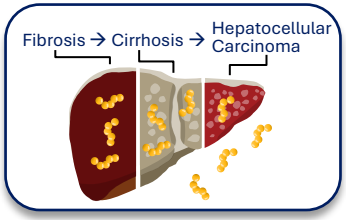
- AATD is a rare, inherited genetic disorder that is commonly caused by a G-to-A point mutation in the SERPINA1 gene
- Pi*ZZ genotype is leading cause of severe AATD, predisposing to progressive lung damage, liver damage or both
- Aggregation of mutant Z-AAT protein in hepatocytes and a lack of functional, wild-type M-AAT drives liver and lung disease, respectively

AATD Lung Disease



- **Treatment goal:** Minimize episodic exacerbations and associated damage
- Lung damage occurs during exacerbations that induce an inflammatory acute phase response, when more AAT protein is needed for protection
- **Weekly IV augmentation therapy is only treatment option**
  - No protective increase in AAT protein levels during acute phase response without additional IV infusions

AATD Liver Disease



- **Treatment goal:** Decrease Z-AAT protein
- Progressive liver disease results from Z-AAT-induced proteotoxic stress
- **No approved therapies**

~200K people in the US and Europe are homozygous for the Z allele (Pi*ZZ genotype)

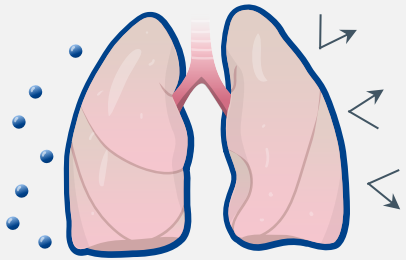
Strnad et al., 2020 *N Engl J Med* 382:1443-55; Blanco et al. 2017 *Int J Chron Obstruct Pulmon Dis* 12:561-69

WVE-006: Potential first-in-class, convenient therapy for AATD that addresses both liver and lung manifestations of the disease

WVE-006 (RNA editing)

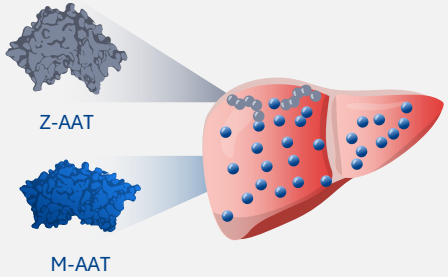
- Proprietary chemistry
- Highly specific (no bystanders)
- Subcutaneous delivery (GalNAc)
- Infrequent dosing

Restore circulating M-AAT and physiological AAT protein production



M-AAT reaches lungs to protect from proteases and **reduce risk of lung pathology**

Reduce Z-AAT protein aggregation in liver



RNA correction replaces mutant Z-AAT protein with wild-type M-AAT protein to **reduce risk of liver pathology**

Strnad et al., 2020 *N Engl J Med* 382:1443-55; Stoller et al., 1993 Alpha-1 Antitrypsin Deficiency GeneReviews. M-AAT: Wild-type alpha-1 antitrypsin protein Z-AAT: mutant alpha-1 antitrypsin protein

RNA editing aims to increase M-AAT and restore physiological AAT production during acute phase response

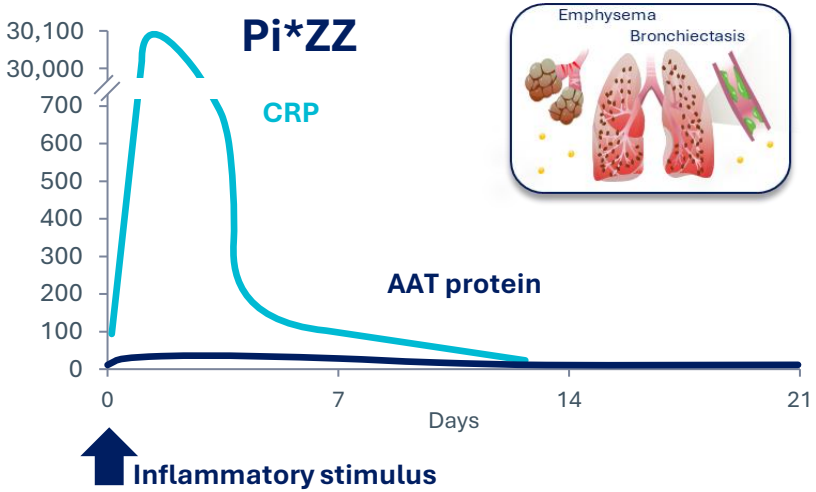
Genotype	Null	Pi*ZZ	Pi*MZ	Pi*MM
	No AAT protein	100% Z-AAT	Z-AAT and M-AAT	100% M-AAT
AAT levels increase during acute phase response	No	No	Yes	Yes
Risk of lung disease	Very high	High	Low	Normal
Risk of liver disease	None	High	Low	Normal

>50% RNA editing
>11 µM AAT

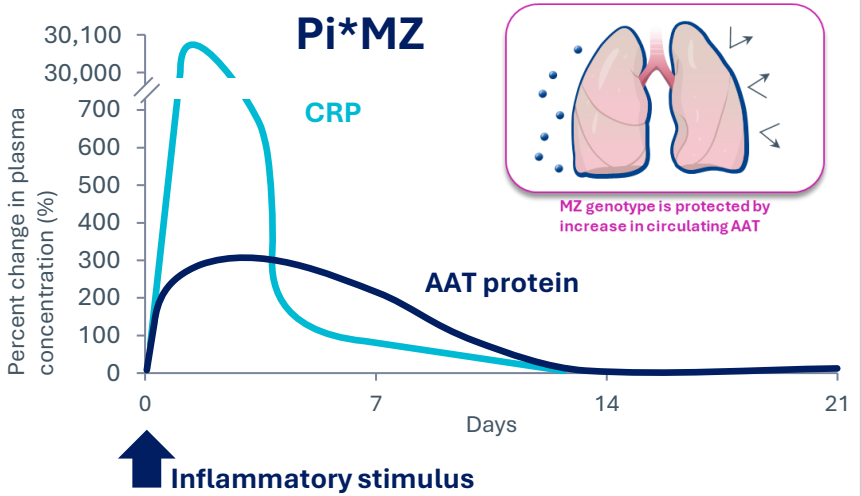
Goal: Shift Pi*ZZ individuals to AAT biomarker profile consistent with Pi*MZ genotype

RNA editing aims to restore production of dynamic and therapeutically relevant levels of AAT protein in Pi*ZZ individuals during acute phase response

Lung damage occurs during exacerbations, when more AAT protein is needed for protection



AAT protein has protective functions and is produced during acute phase response



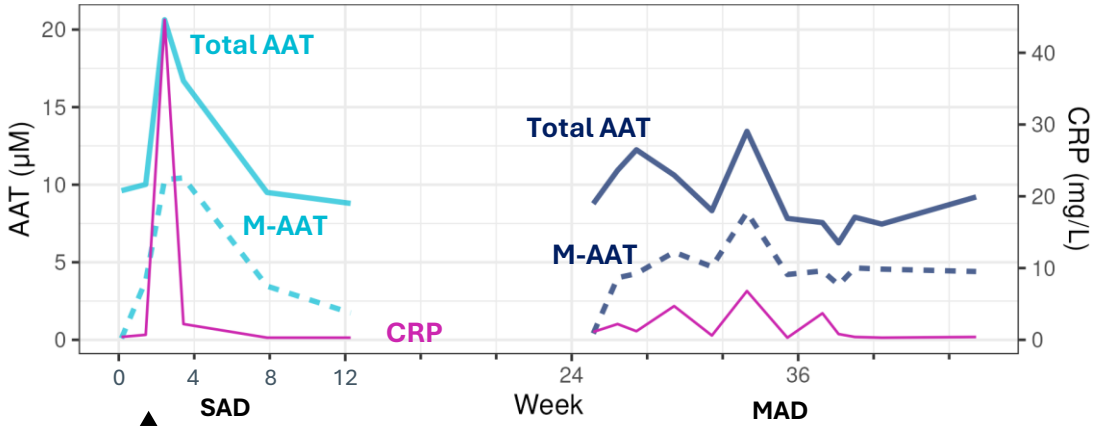
RNA editing has potential to restore dynamic AAT response to inflammation

Left: Mantovani A, Garlanda C. *N Engl J Med*, 2023;388:439-452; Right: Sanders et al., *J COPD*, 2018

First-ever demonstration of ability to restore physiological serum AAT production; total AAT reached 20.6 µM during acute phase response

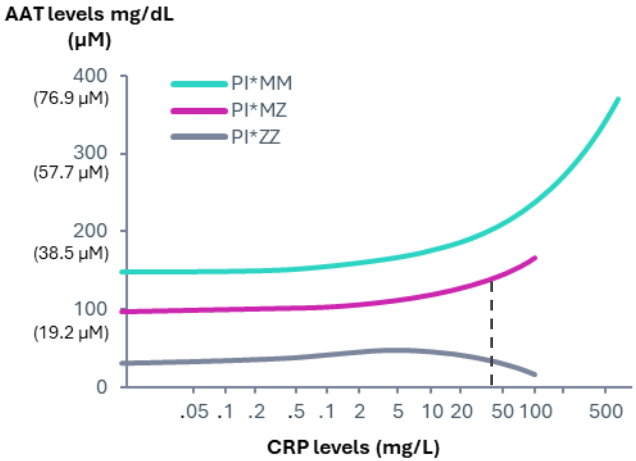
Pi*ZZ patients have a reduced capacity to produce AAT protein during an acute phase response

Following WVE-006 200 mg single dose, total AAT and M-AAT increased significantly in one patient during an acute phase response



▲ Acute phase response due to a kidney stone

Published data[1] on CRP levels and AAT levels across different genotypes



AAT response in Pi*ZZ participant treated with WVE-006 mirrors Pi*MZ phenotype

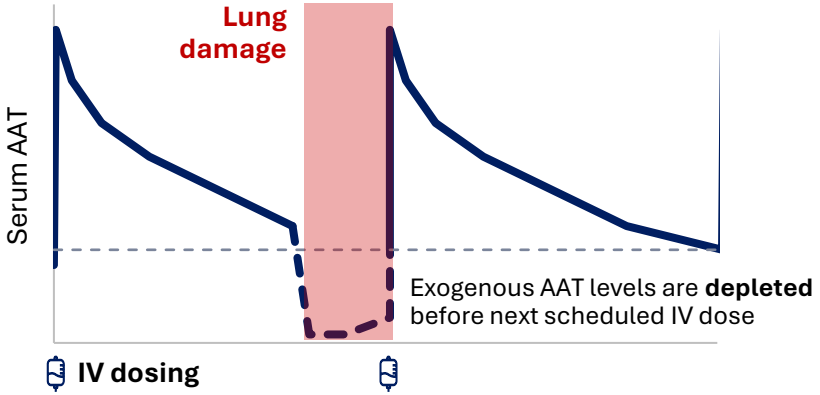
1 - Sanders et al., J COPD, 2018 CRP: C-reactive protein

Circulating M-AAT, Z-AAT, and total (M + Z) AAT protein in the serum were measured by highly selective and sensitive LC-MS/MS assays (LLOQ: 0.096 µM (M), 0.029 µM (Z)) and reported as mean participant SAD and MAD maximums

WVE-006 enables endogenous AAT production during an acute phase response while augmentation therapy may leave patients at risk

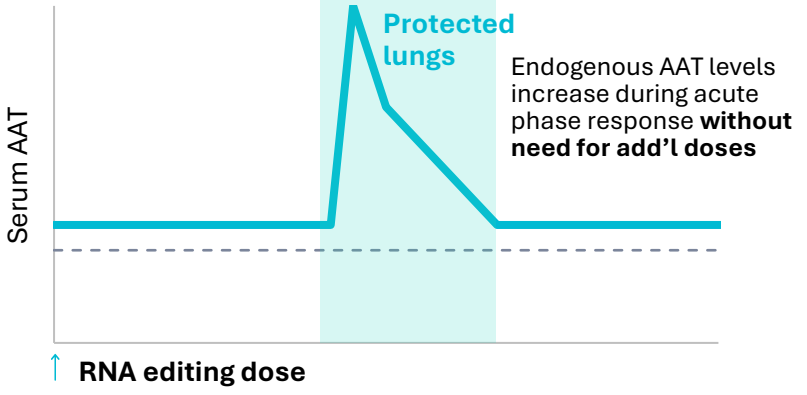
Illustrative model of impact of acute phase response

Augmentation therapy



- Augmentation therapy has **no impact** on liver disease

WVE-006 treatment approach



- WVE-006 also reduces levels of Z-AAT

WVE-006 therapeutic goal is to restore dynamic AAT physiology; augmentation therapy goal is to maximize AAT levels as dynamic response is not enabled

WVE-006 achieved key treatment goals of restoring MZ phenotype

Total AAT levels exceeded 11 µM, production of wild-type M-AAT of greater than 50%, restored physiological AAT production

Plasma AAT of ~13 µM

- Protein levels associated with lower risk of AATD liver and lung diseases

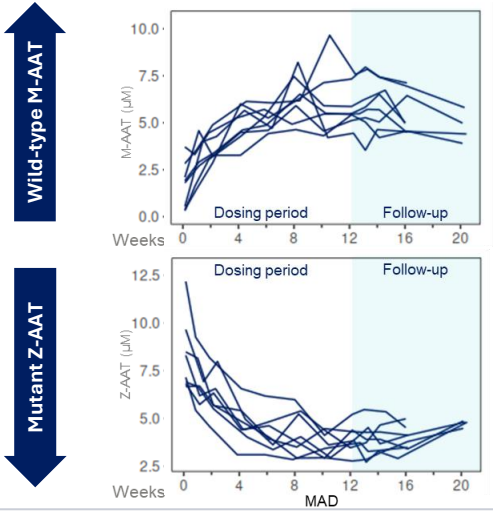
400 mg single dose

12.8 µM total AAT

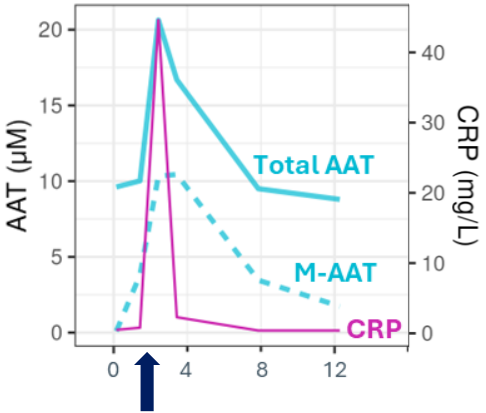
200 mg bi-weekly

11.9 µM total AAT

Wild-type M-AAT protein of 64% of total, reduction in Z-AAT



AAT reached >20 µM during an acute phase response



400 mg monthly and 600 mg single dose data expected in May 2026

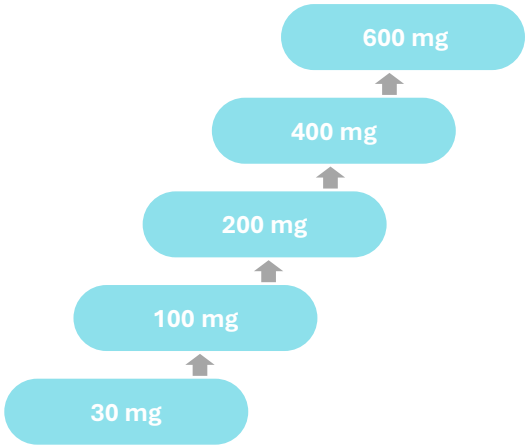
Circulating M-AAT, Z-AAT, and total (M + Z) AAT protein in the serum were measured by highly selective and sensitive LC-MS/MS assays (LLOQ: 0.096 µM (M), 0.029 µM (Z)) and reported as mean participant SAD and MAD maximums. Middle: from 200 mg MAD cohort; Right: from 200 mg SAD cohort.

RestorAATion-2 clinical trial ongoing

RESTORAATION

RestorAATion-1: Healthy Volunteers → **RestorAATion-2: AATD Patients**

SAD → MAD Multi-dosing complete



SAD Cohort 3
600 mg → **MAD Cohort 3**
600 mg; Q4W

SAD Cohort 2
400 mg → **MAD Cohort 2**
400 mg; Q4W

SAD Cohort 1
200 mg → **MAD Cohort 1**
200 mg Q2W

Study key objectives		
Safety and tolerability	Pharmacokinetics	Serum M-AAT levels

HV: healthy volunteer; SAD: single-ascending dose; MAD: multi-ascending dose

WVE-008
RNA editing (AIMer)

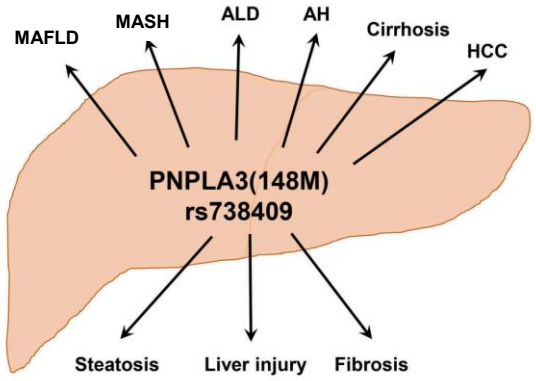
PNPLA3 I148M liver disease

WAVE LIFE SCIENCES

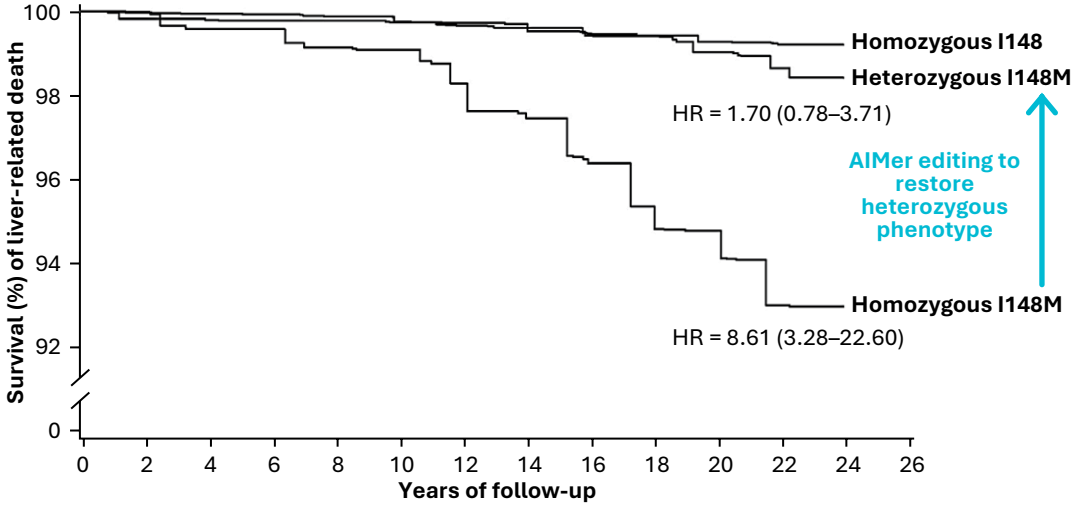
WVE-008 for PNPLA3 I148M liver disease

GalNAc-RNA editing approach uniquely aims to restore PNPLA3 function to fully address disease

Homozygous PNPLA3 I148M carriers have significantly higher risk of multiple liver diseases



Heterozygous carriers have 80% lower risk of liver-related death as compared to homozygous carriers



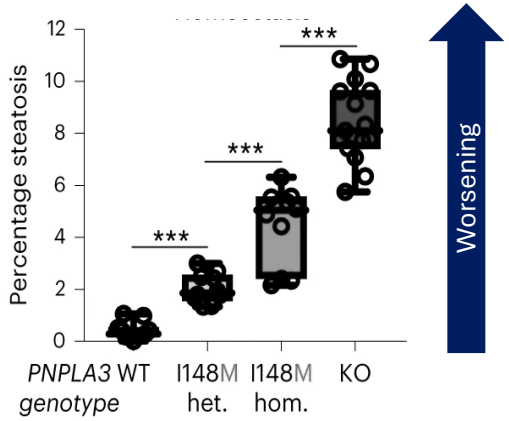
Over nine million homozygous PNPLA3 I148M patients with liver disease in US and Europe

1. Carlsson, B., et al. 2020 *Aliment Pharmacol Ther.*; 2. Unalp-Arida and Ruhl 2020 *Hepatology*; 3. Dong, XC, 2019 *Front. Med*. 4. Liver International, 2025; 45:e16133

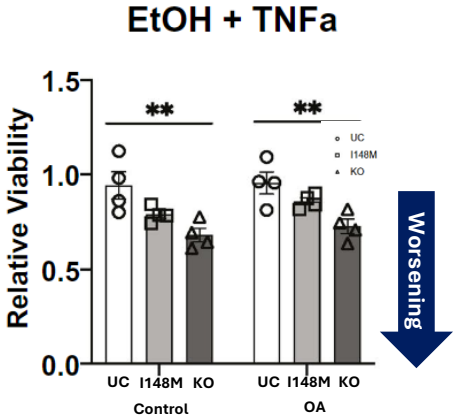
MAFLD, Metabolic dysfunction-associated fatty liver disease; MASH, Metabolic dysfunction-associated steatohepatitis; ALD, alcoholic liver disease; AH, Alcohol-associated hepatitis; HCC, hepatocellular carcinoma

Silencing of PNPLA3 in normal liver may worsen basal physiological functions

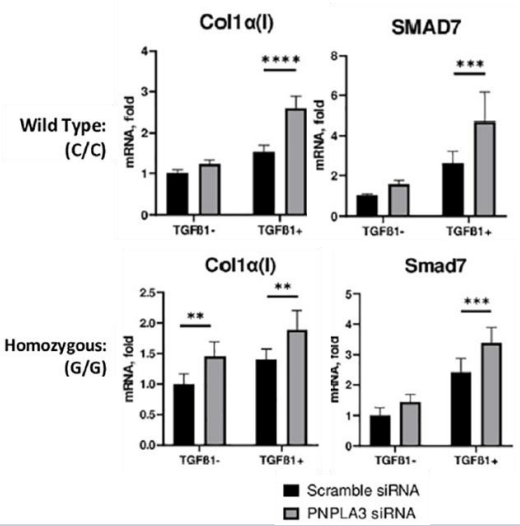
Silencing PNPLA3 worsens steatosis in iPSC-derived human liver organoids[2]



Silencing PNPLA3 increases inflammation-induced liver cell death in human primary hepatocytes[3]



PNPLA3 siRNA exacerbates the fibrotic response in hepatic stellate cells[1]



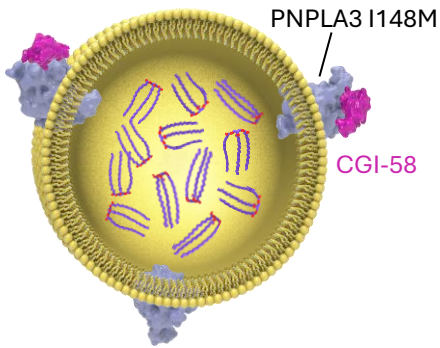
Functional PNPLA3 is imperative for liver health beyond improvements in steatosis

1. Rady, B, et al. 2021 PLoS ONE 2021; 2. Hendriks, D, et al. 2023 Nat Biotechnol; 3. Tilson, SG, et al. 2021 Hepatology

RNA editing is expected to restore PNPLA3 function to treat across the stages of liver diseases

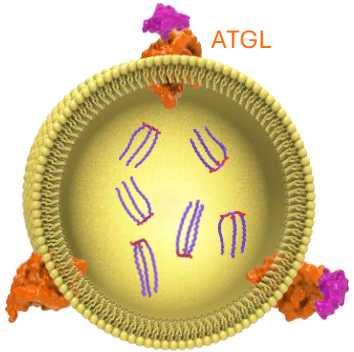
RNA editing approach

PNPLA3 I148M aggravates steatosis and fibrosis through gain-of-function



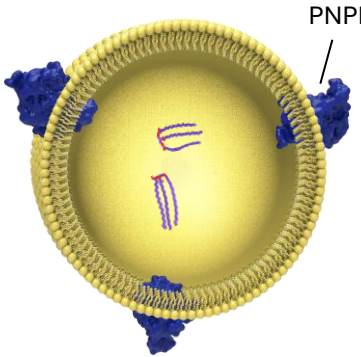
- PNPLA3 I148M accumulates on LDs, sequesters CGI-58, inhibits ATGL's lipase activity and lipid mobilization from ER
- Suppresses retinol metabolism in liver and worsens inflammation and fibrosis
- Promotes liver fat accumulation and fibrosis through activation of stellate cells

Silencing PNPLA3 may only partially address disease



- Creates PNPLA3 loss of function
- ATGL partial rescue for loss PNPLA3
- Silencing will not restore retinol metabolism
- **Fibrosis, ballooning, and inflammation persist**

PNPLA3 correction expected to restore function, counter liver disease



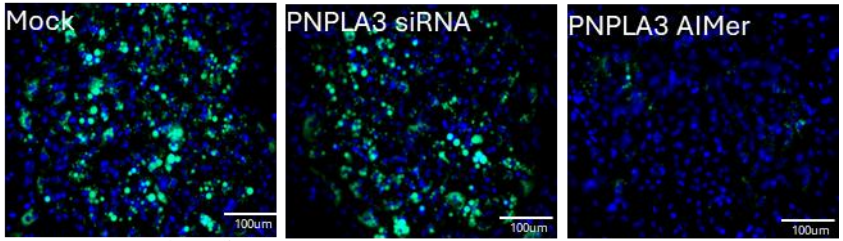
- Restores full PNPLA3 activity
- **Restores lipid mobilization, reverses steatosis, fibrosis, ballooning, and inflammation**

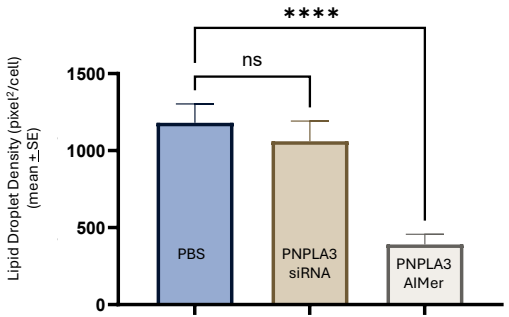
ATGL: adipose triglyceride lipase; CGI-58: co-factor for ATGL; ER endoplasmic reticulum; LDs: lipid droplets; CGI-58 also called ABHD5

Liver International, 2025; 45:e16117; Human Molecular Genetics, (2014) 23(15): 4077–4085

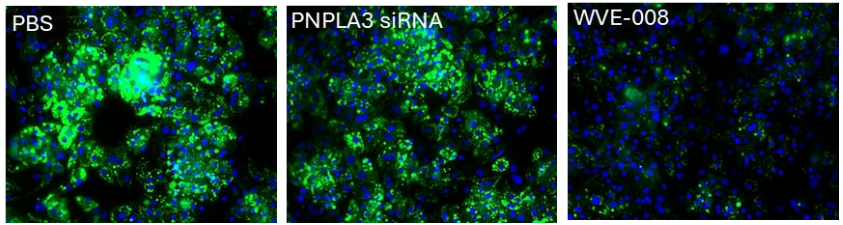
AIMers achieve efficient editing of PNPLA3, leading to reduction of liver fat

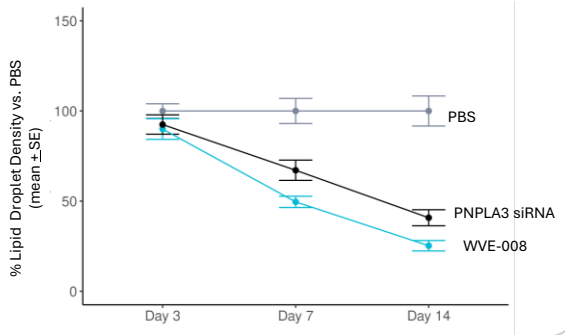
Significant decrease in liver fat with PNPLA3 editing in human HEPATOPAC® model with homozygous I148M





Decrease in liver fat with WVE-008 in monolayer model

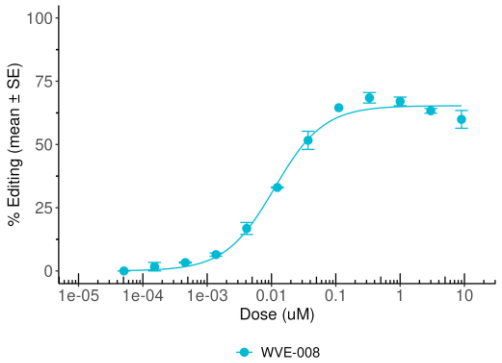




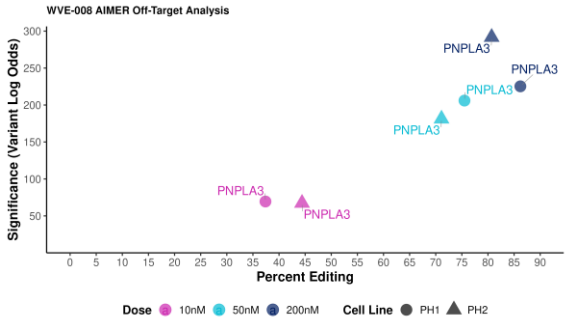
One-way ANOVA with Dunnett post hoc test comparisons to Mock **** P< 0.0001

Preclinical data support WVE-008 as potential first-in-class, disease modifying therapy, for treatment of PNPLA3 I148M liver disease

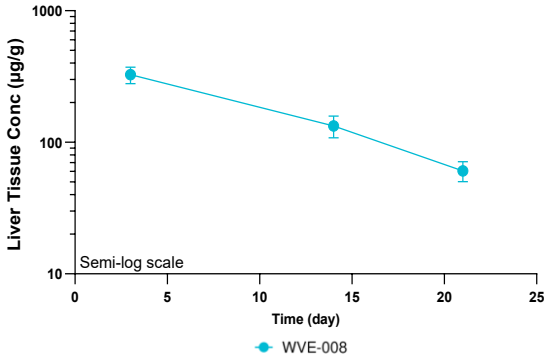
Potential editing with WVE-008



Highly specific editing with WVE-008



Tissue exposure supports excellent delivery



Expect to file Clinical Trial Application (CTA) for WVE-008 in 2026

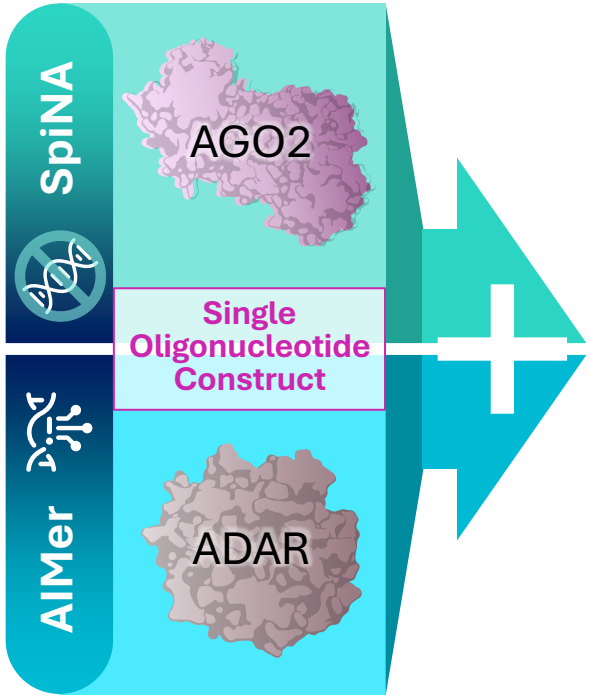
Left: 4-parameter log-logistic dose response curve; Middle: Analysis utilized RNA-sequencing with two separate primary human hepatocyte cell lines (PH1/2). Variant calling utilized GATK best practices for RNA variant calling using Mutect2 and display A->G evidence found when filtering for variants found in both cell lines and all doses.

Bifunctional modalities

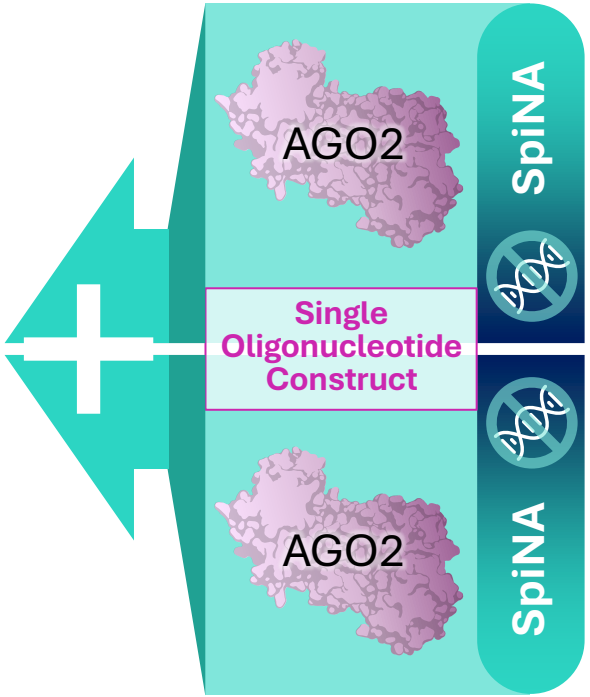
Single oligonucleotide constructs

WAVE® LIFE SCIENCES

Reimagining RNA medicines: Bifunctional modalities



- ✓ Engage both endogenous Ago2 and ADAR enzymes, as well as dual RNAi silencing
- ✓ Silence multiple targets or silence one target while simultaneously editing or upregulating another unique target
- ✓ Unlock complex indications that require engaging multiple targets
- ✓ May continue to increase durability of editing



Other clinical programs

Duchenne muscular dystrophy

WAVE® LIFE SCIENCES

Advancing WVE-N531 in exon 53 amenable DMD

WVE-N531: exon skipping oligonucleotide designed to induce production of endogenous, functional dystrophin protein

- High unmet need for therapies delivering **more consistent dystrophin expression,** as few patients today achieve dystrophin >5% of normal
- **Opportunity to extend dosing intervals** beyond weekly standard of care to alleviate burden for patients and caregivers
- **Need to reach stem cells and distribute broadly to muscle tissues** to potentially enable muscle regeneration and impact respiratory and cardiac function
- WVE-N531 has Rare Pediatric Disease Designation and Orphan Drug Designation from FDA

DMD impacts ~1 / 5,000 newborn boys annually; ~20,000 new cases annually worldwide

WAVE LIFE SCIENCES

Duan, D. et al. 2021 Nat Rev Dis Primers 7, 13; Muscular Dystrophy Association; Aartsma-Rus, et al. 2009 Hum Mutat 30, 293.

FORWARD-53 48-week clinical trial results: WVE-N531's potential best-in-class profile for boys amenable to exon 53 skipping

- Statistically significant and clinically meaningful improvement (3.8s) in Time-to-Rise vs. natural history; functional benefits on other measures including NSAA
- Statistically significant reductions in muscle fibrosis and CK; driven by decreases in inflammation and necrosis; transition from regenerative to mature muscle
- Consistent dystrophin expression averaged 7.8% between 24 and 48 weeks, with 88% of boys above 5% dystrophin; delivery to both myofibers and muscle stem cells
- WVE-N531 remains generally safe and well-tolerated with no Serious Adverse Events

NDA filing for accelerated approval with monthly dosing planned for 2026

Reimagining RNA medicines

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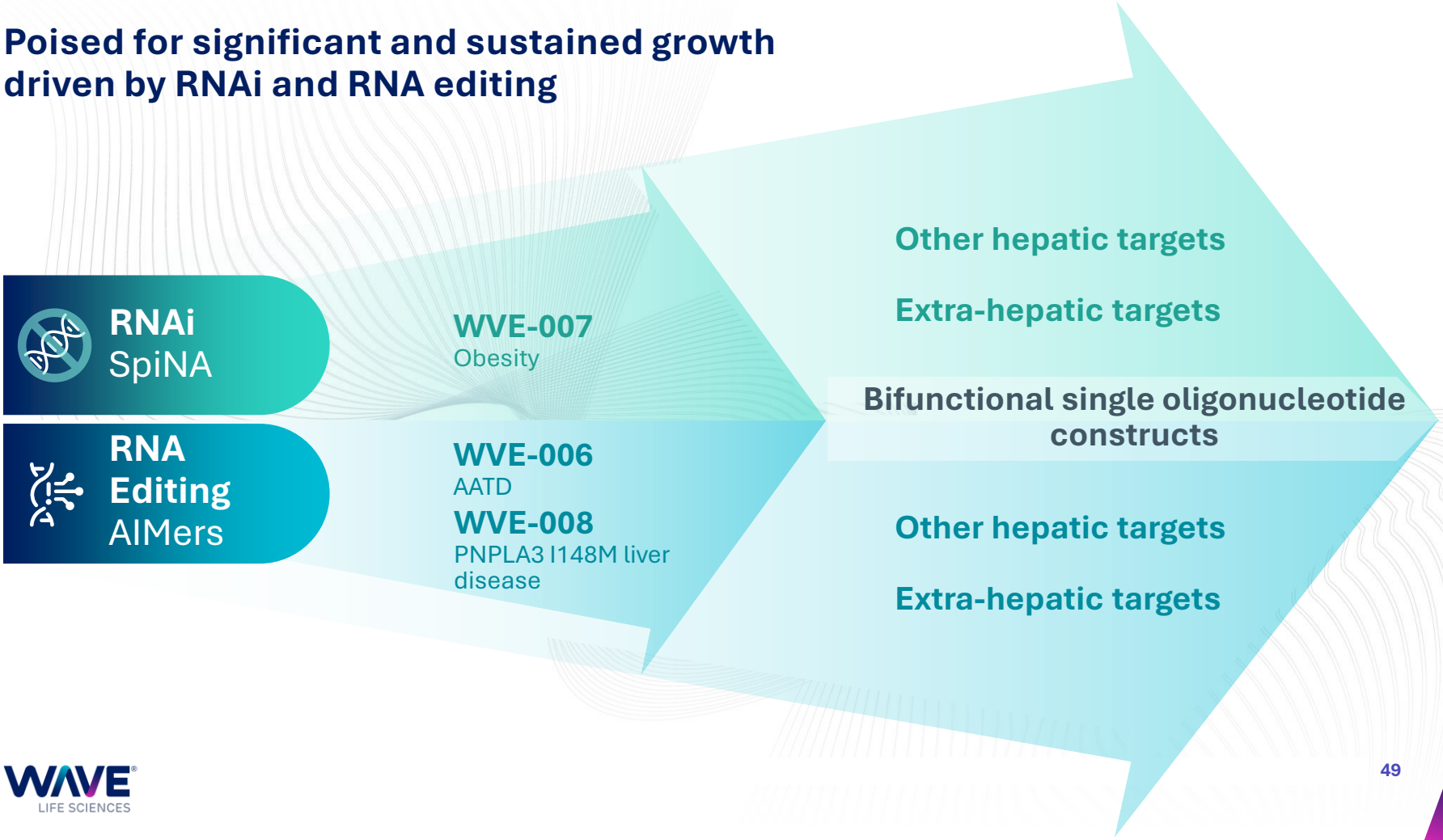
Poised for significant and sustained growth driven by RNAi and RNA editing



Anticipated upcoming milestones

WVE-007
(INHBE)
Obesity

- Deliver additional data from INLIGHT, including data from the 600 mg SAD cohort in 2026
- Initiate Phase 2a multidose portion of INLIGHT in individuals living with obesity with higher BMI with and without type 2 diabetes in 2Q 2026
- Combination and maintenance studies of WVE-007 expected to initiate in 2026

INLIGHT

WVE-006
(SERPINA1)
AATD

- Deliver data from 400 mg MAD cohort and 600 mg SAD cohort in May 2026
- Deliver multidose data from 600 mg cohort in 2H 2026
- Regulatory feedback on potential accelerated approval pathway expected mid-2026

RESTORAATION

WVE-008
PNPLA3 I148M liver disease

- File CTA for WVE-008 in 2026

WVE-N531
(exon 53)
DMD

- Submit NDA to support accelerated approval of WVE-N531 with monthly dosing in 2026

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BMI: body mass index AATD: alpha-1 antitrypsin deficiency DMD: Duchenne muscular dystrophy CTA: Clinical Trial Application NDA: New Drug Application.

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Reimagine possible.

For questions contact:
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