Wave Life Sciences

Corporate Presentation

July 30, 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

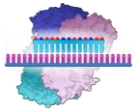
Differentiated RNA medicines platform and chemistry

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

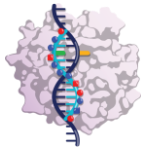
RNAi



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

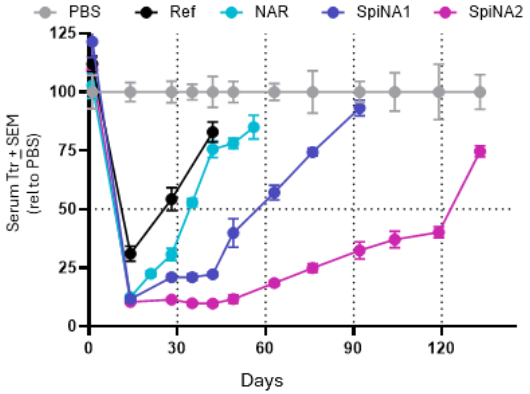
- **Extra-hepatic capabilities:** with RNAi and RNA editing
- **Bifunctional modalities:** single oligonucleotide constructs for dual RNAi silencing or RNAi silencing + RNA editing

Well capitalized with expected cash runway into 3Q 2028

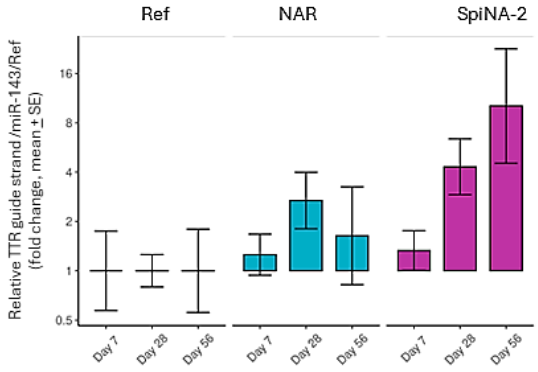
For over a decade Wave has been extending the frontiers of RNA therapies delivering breakthroughs in nucleic acid chemistry

RNAi — SpiNA

Protein reduction

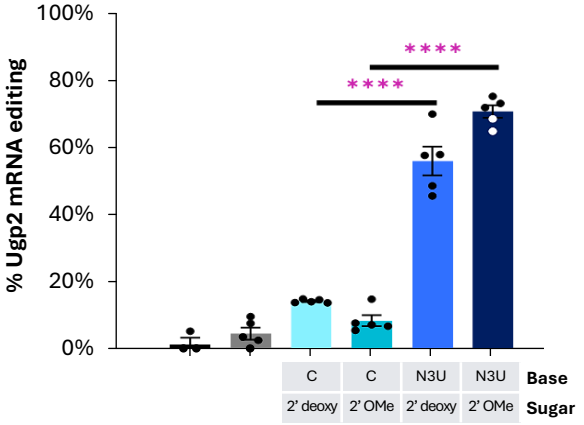


Ago2 loading



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

RNAi (SpiNA)

Program	Discovery	IND / CTA Enabling Studies	Clinical	Patient population
WVE-007 (GalNAc) INHBE (obesity)	**INLIGHT™ trial (monotherapy)**			**175M** **(>1 billion globally)**
	Combination with incretins			
	Post-incretin maintenance			
GalNAc / extra-hepatic Multiple				--

RNA editing (AIMer)

Program	Discovery	IND / CTA Enabling Studies	Clinical	Patient population
WVE-006 (GalNAc) SERPINA1 (AATD)	**RestorAATion-2 trial**			**200K**
WVE-008 (GalNAc) PNPLA3 (liver disease)				**9M**
GalNAc / extra-hepatic Multiple				--

Other pipeline programs

Program	Discovery	IND / CTA Enabling Studies	Clinical	Patient population
WVE-N531 Exon 53 (DMD)				**2.3K**
WVE-003 mHTT (HD)				**25K Symptomatic (SNP3)** **60K Pre-Symptomatic (SNP3)**

WAVE LIFE SCIENCES

Patient population includes US and Europe
AATD: Alpha-1 antitrypsin deficiency; DMD: Duchenne muscular dystrophy; HD: Huntington's disease

WVE-007
GalNAc-siRNA silencing

Obesity

WAVE LIFE SCIENCES

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

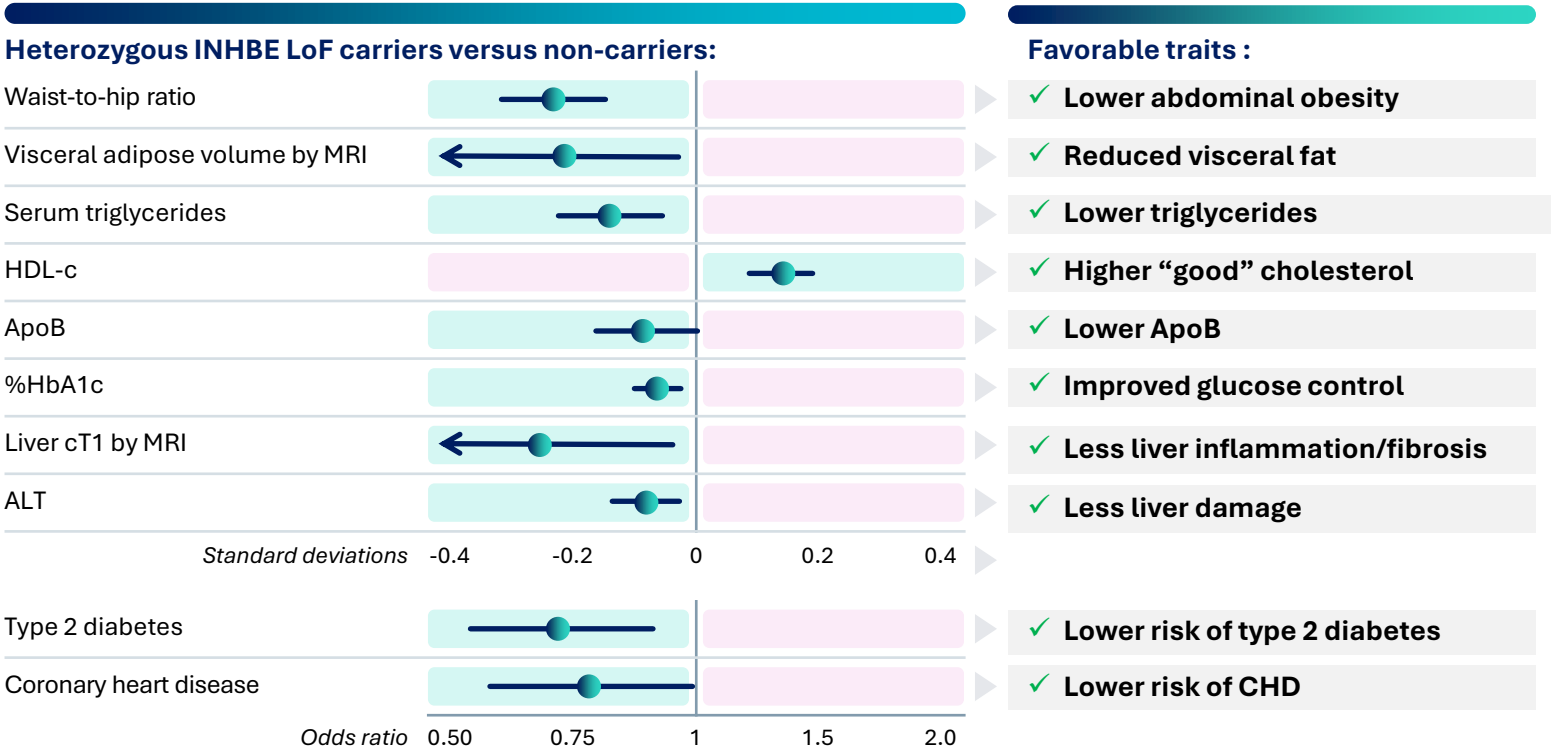
Focused on adipocyte lipolysis and not caloric deficit

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

WAVE LIFE SCIENCES

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.

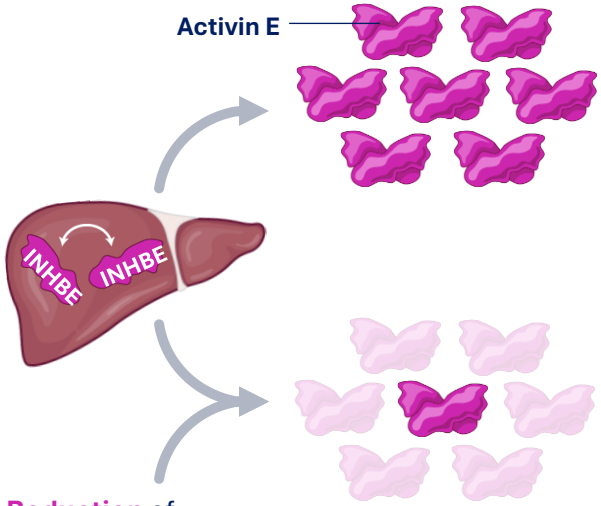
Human genetic data demonstrate that heterozygous INHBE loss-of-function (LoF) carriers have lower visceral fat and a healthier metabolic profile



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

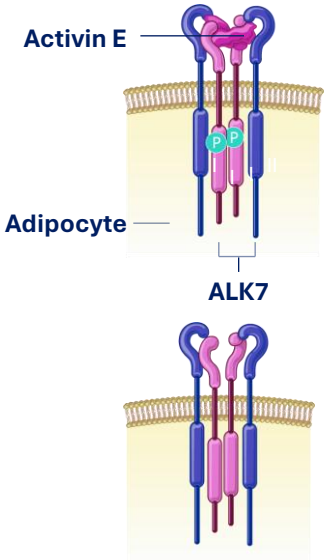
Release of **dimerized** INHBE subunits creates hepatokine **Activin E**



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

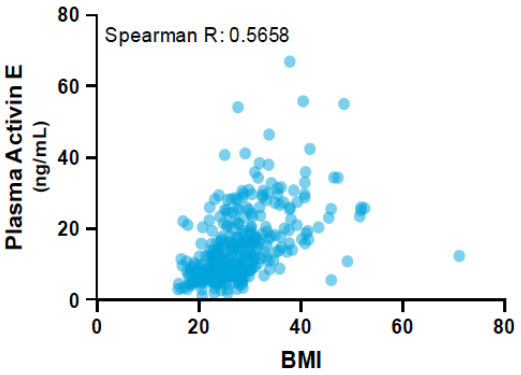
Increased abdominal adiposity leads to **obesity, CVD and T2D**

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

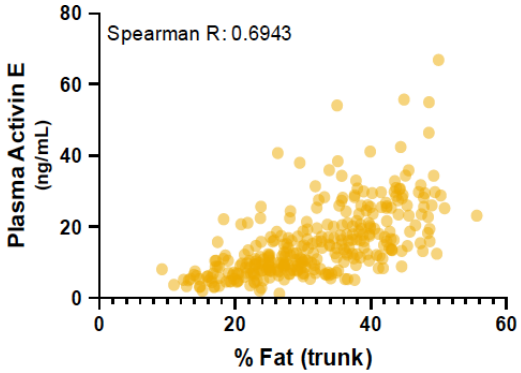
1. Cell Reports (2018) 25, 1193–1203; 2. Biochemical Journal (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8

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

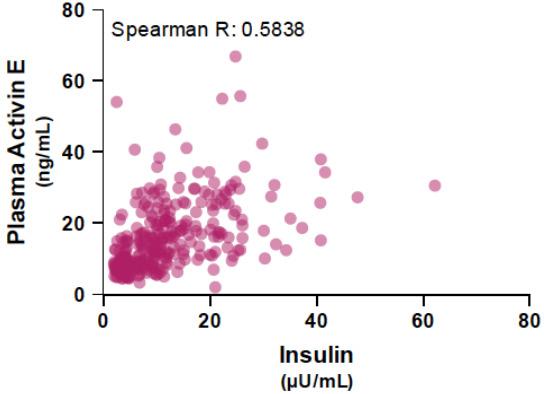
BMI



Abdominal Fat



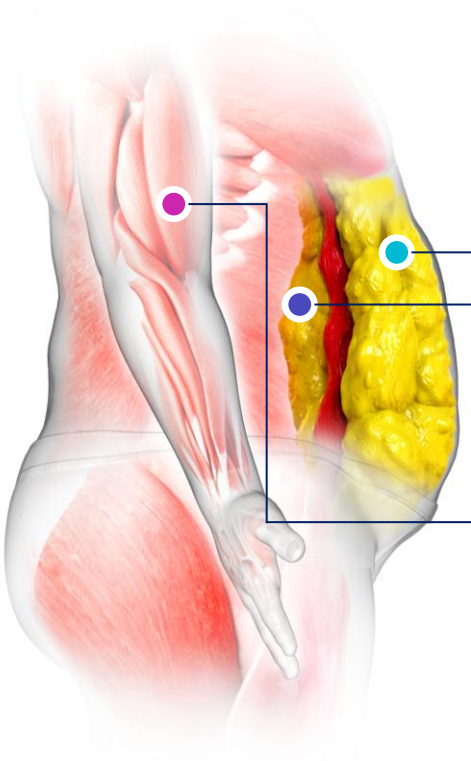
Fasting Insulin



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

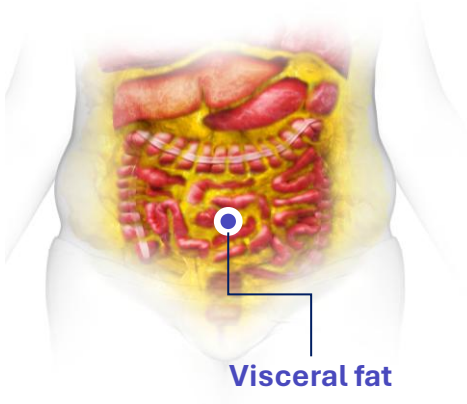
Total Fat REDUCED

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
- PMOS

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

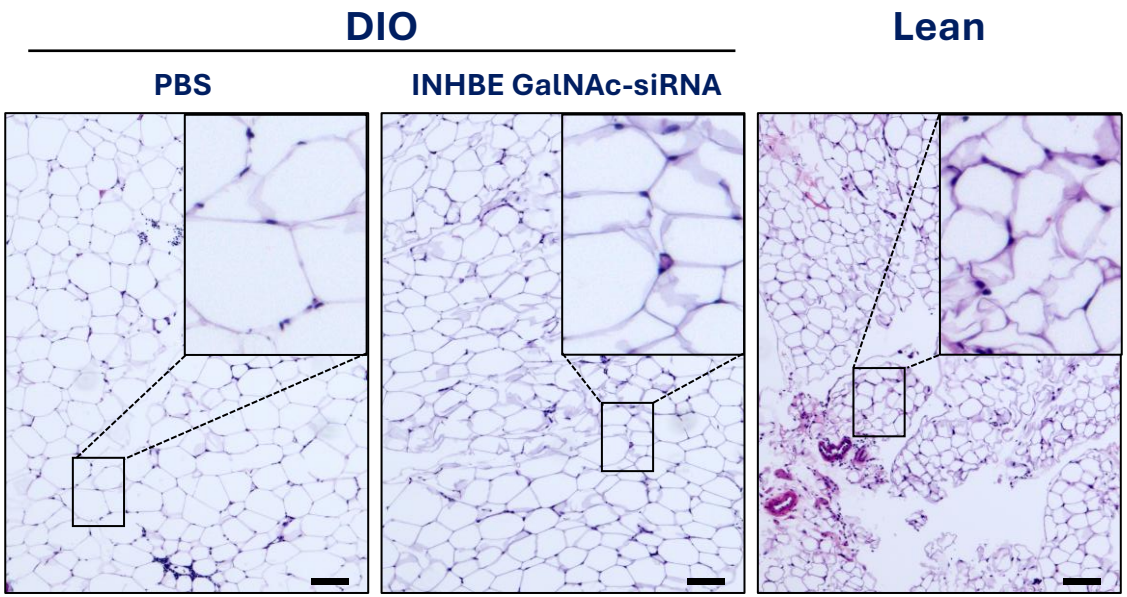
WVE-007 aims to address a key limitation of current standard of care: up to 40% of weight loss is driven by muscle loss

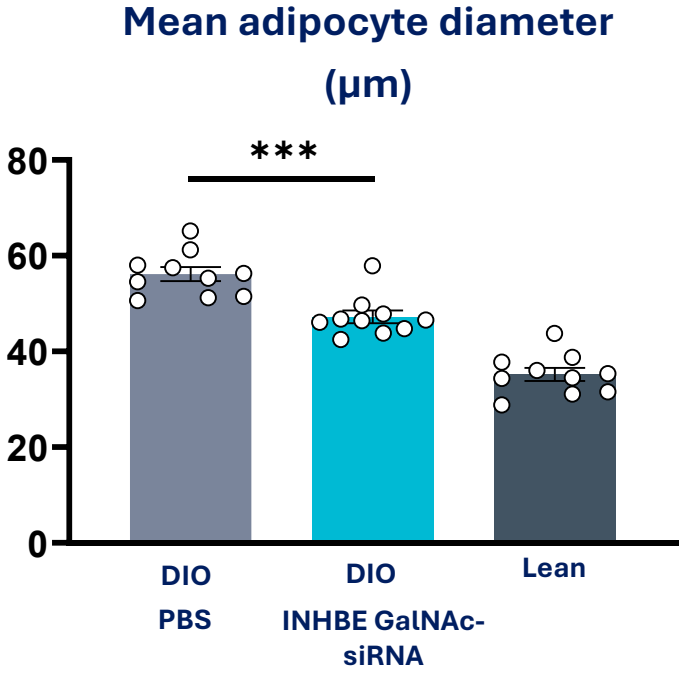
Preservation of muscle mass is linked to many health benefits

- 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

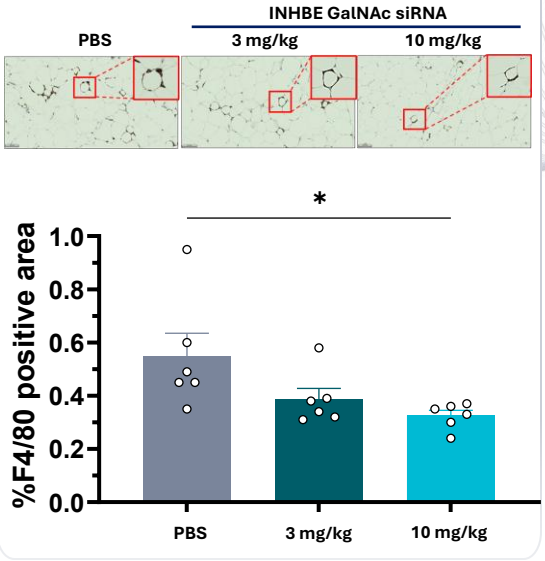




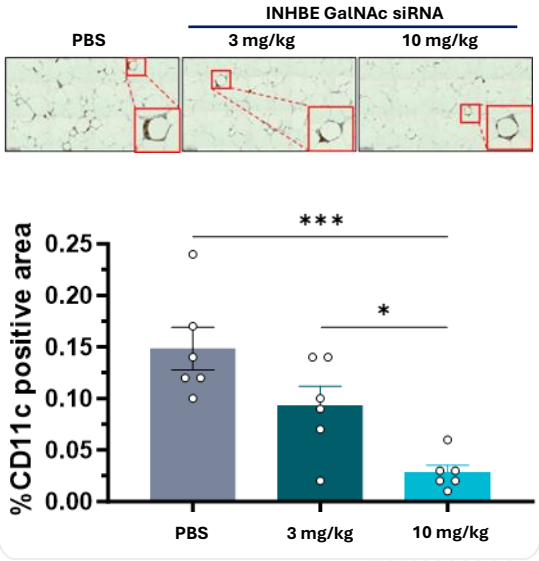
Data presented at ADA Scientific Sessions June 2025
***p<0.001; Day 28

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

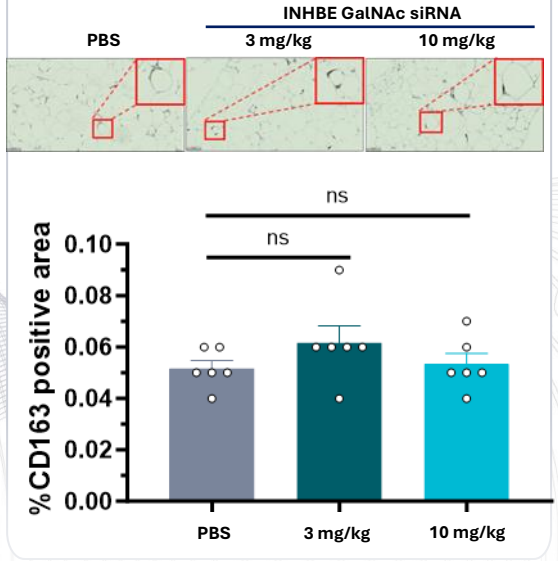
Macrophages (Mϕ) (F4/80)



Pro-inflammatory (M1) Mϕ (CD11c)



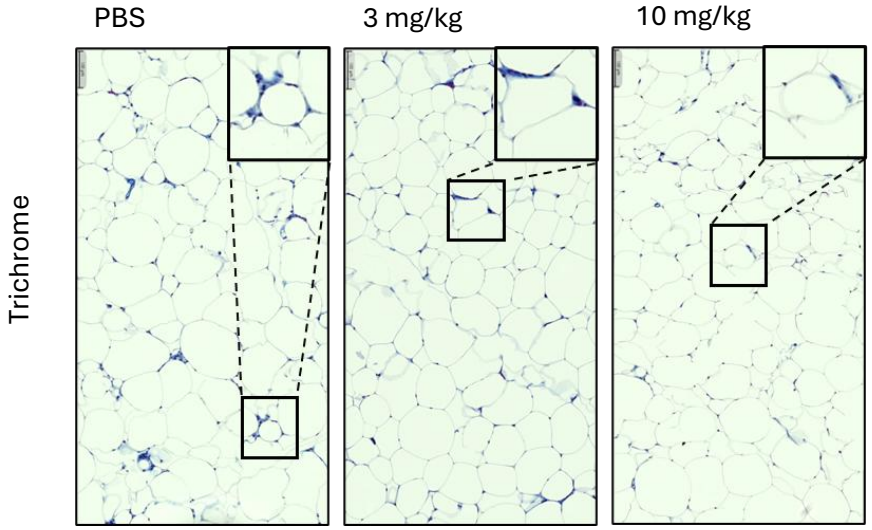
Anti-inflammatory (M2) Mϕ (CD163)



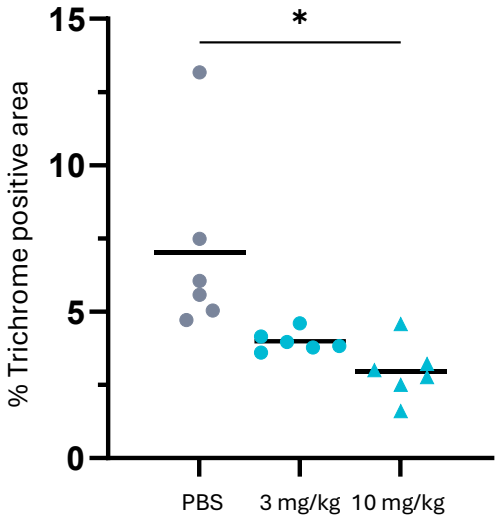
Data presented at ADA Scientific Sessions June 2025
***p<0.001, *p<0.05, ns=non-significant

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

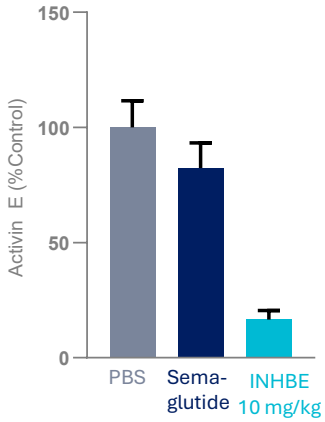
- ↓ Risk of CVD
- ↓ Risk of T2D

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

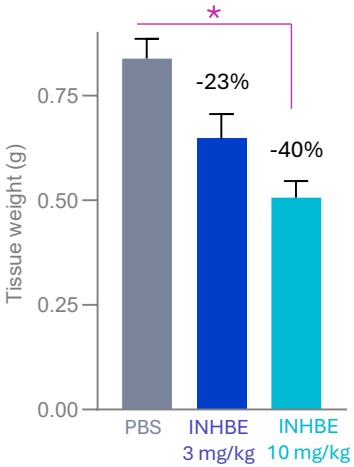
Durable Activin E reduction

Serum Activin E



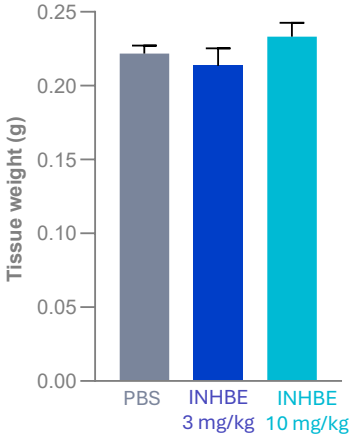
Reduction in fat

Epididymal fat weight



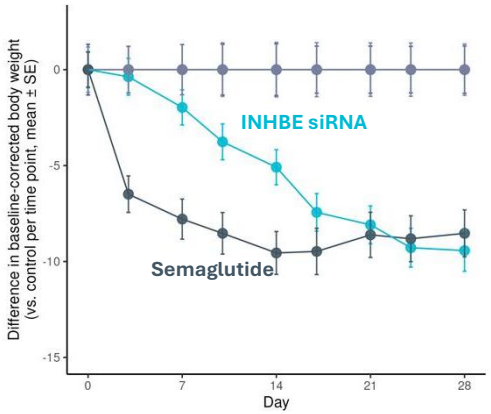
Muscle preservation

Quadricep weight



Reduction in body weight

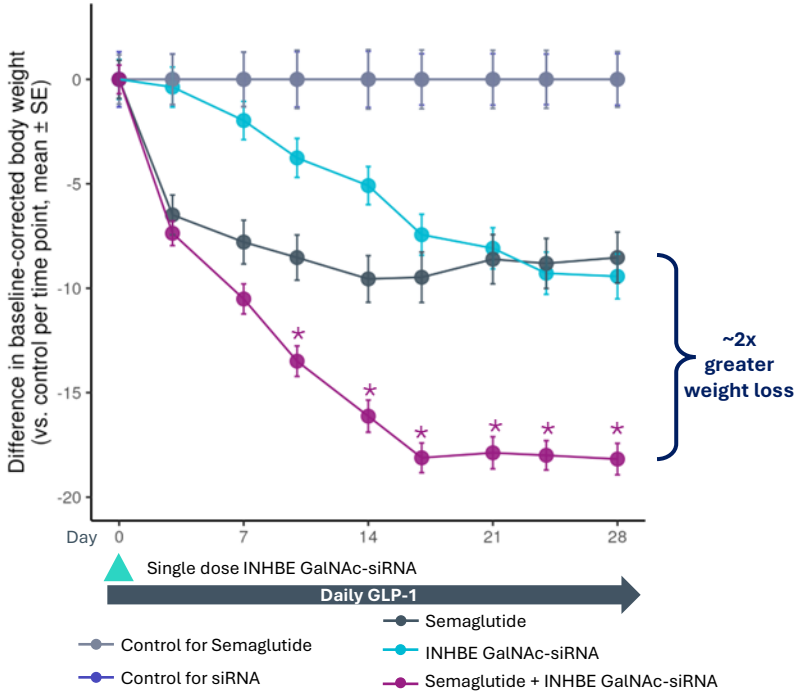
Single dose INHBE GalNAc-siRNA



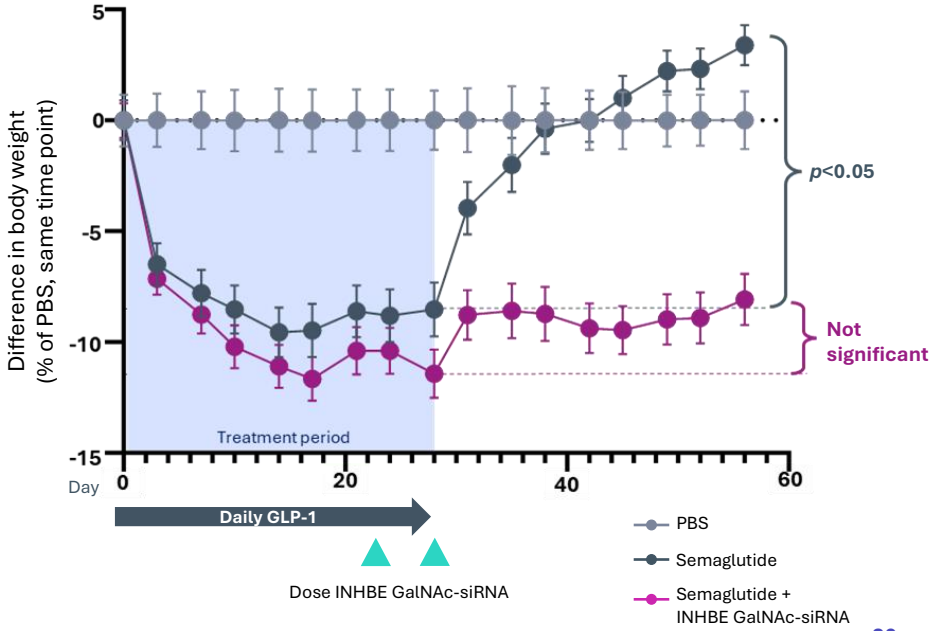
Left and right panels: Semaglutide 10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human; INHBE GalNAc-siRNA 10 mg/kg dose. All data from preclinical studies were conducted in mice fed with 60% high fat diet. Linear Mixed Effects ANOVA with post hoc comparisons of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

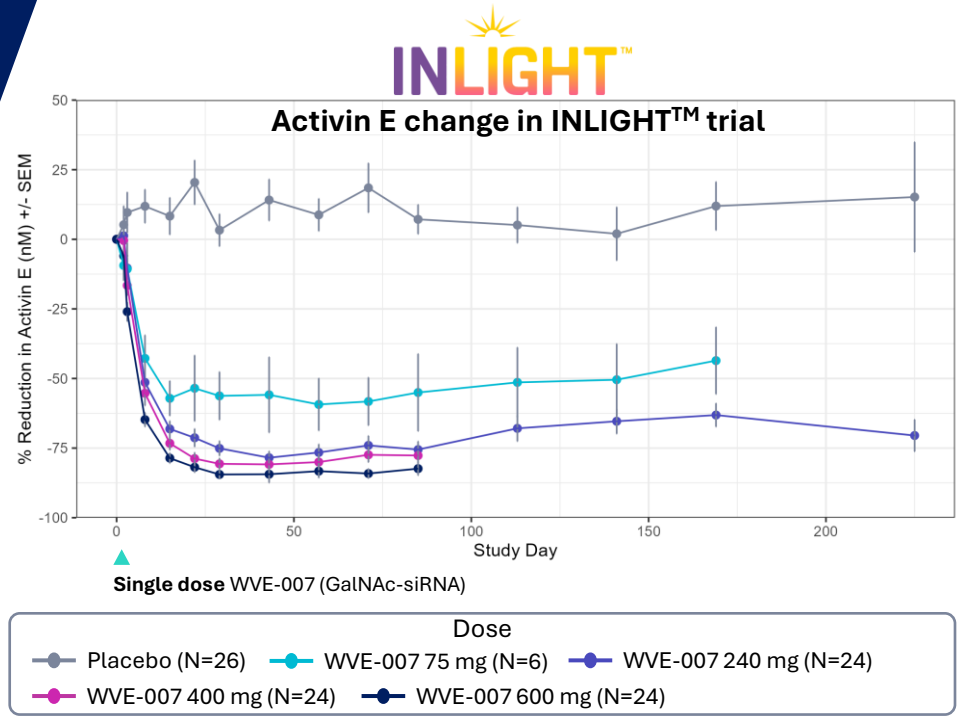
MAD high BMI (35–50 kg/m^2) cohorts

- 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

WAVE LIFE SCIENCES

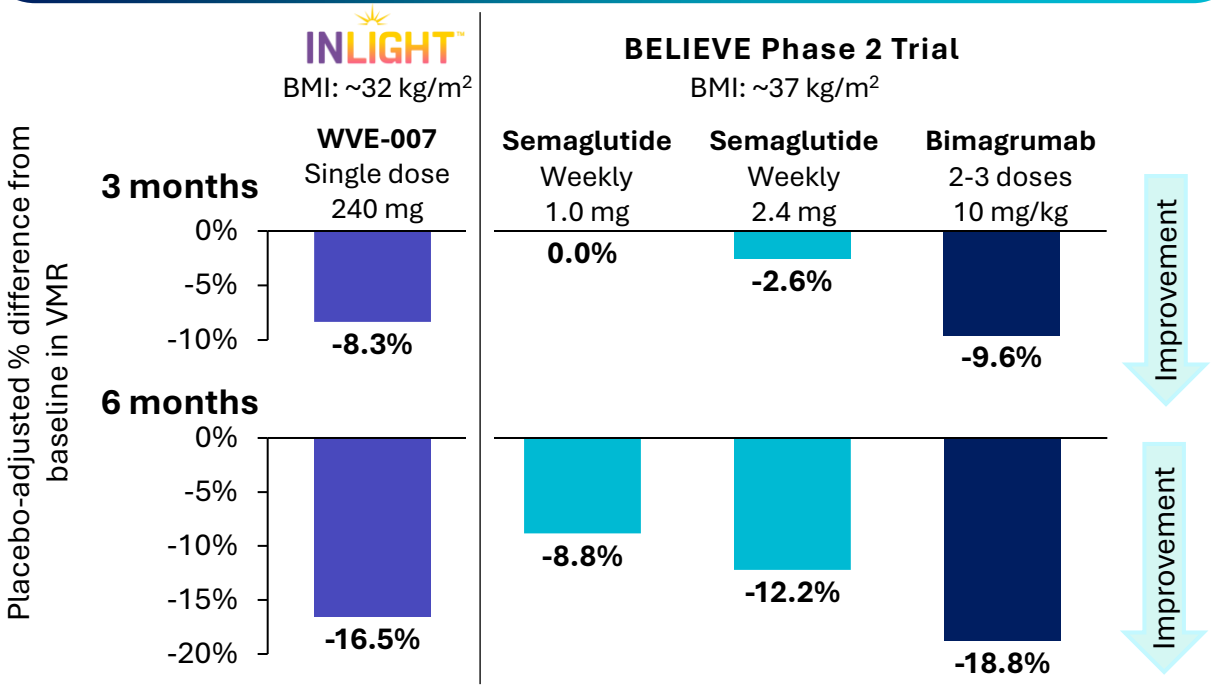
INLIGHT interim Phase 1 data reported March 26, 2026; Left: figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. Right: *p<0.05. All reductions are placebo-adjusted % change from baseline were estimated using an MMRM model with fixed effects for 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]

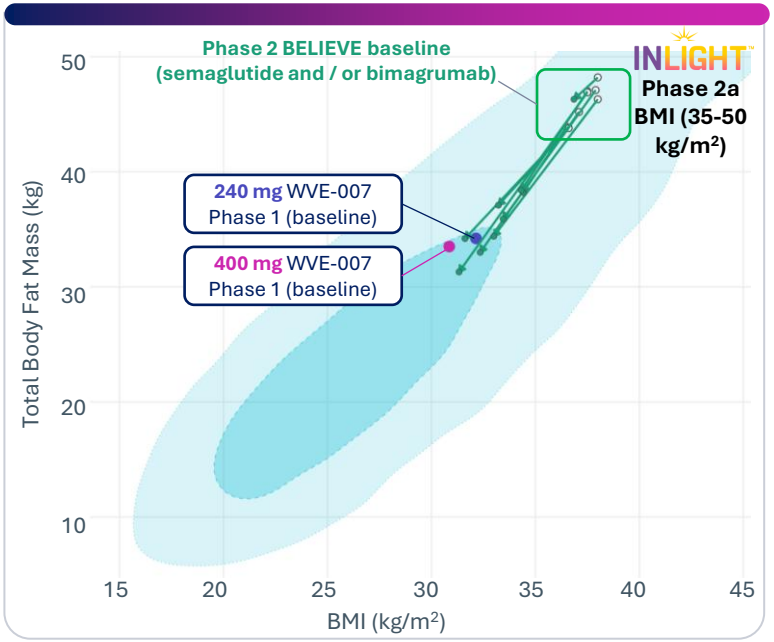


1. Zhang S, *et al.* 2023 *Diabetes Metab Res Rev.* 39(2):e3597; 2. Liu C, *et al.* 2024 *Lipids Health Dis.* 23(1):104; 3. Wang Q, *et al.* 2019 *Diabetes Metab Syndr Obes.* 12:1399-1407. 4. Placebo-corrected VMR calculated based on changes from baseline in visceral fat and lean mass at 3 and 6 mo.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

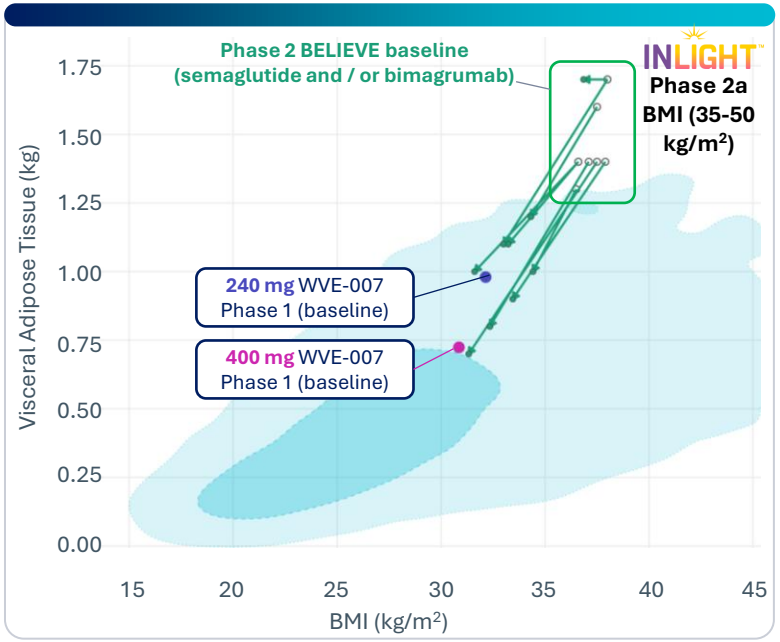
Note: The data presented above are derived from different clinical trials with differences in trial design and patient population, including with respect to BMI. As a result, cross-trial comparisons cannot be made and no head-to-head clinical trials have been conducted.

Phase 2a INLIGHT™ trial: 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)

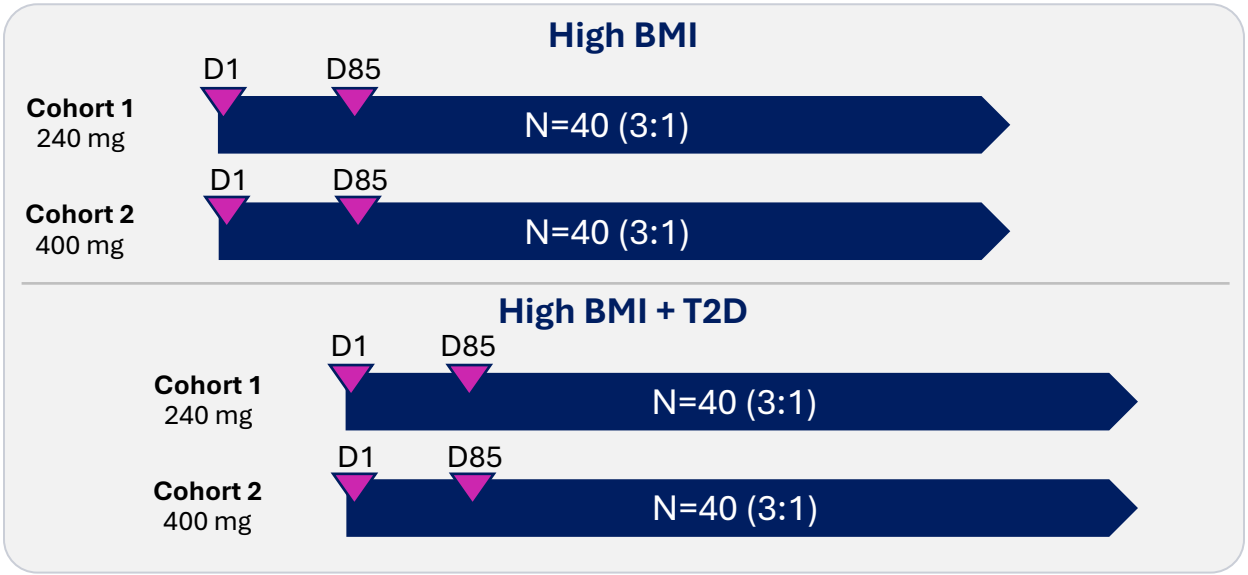
- 50% of population
- 95% of population

Expect greater fat loss in Phase 2a INLIGHT™ trial 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.

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

INLIGHT™



- Individuals with **high 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)

Phase 2a (MAD) portion of INLIGHT™ trial underway

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

Phase 2a portion of INLIGHT™ monotherapy trial underway; combination and maintenance trials of WVE-007 expected to initiate in 2H 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

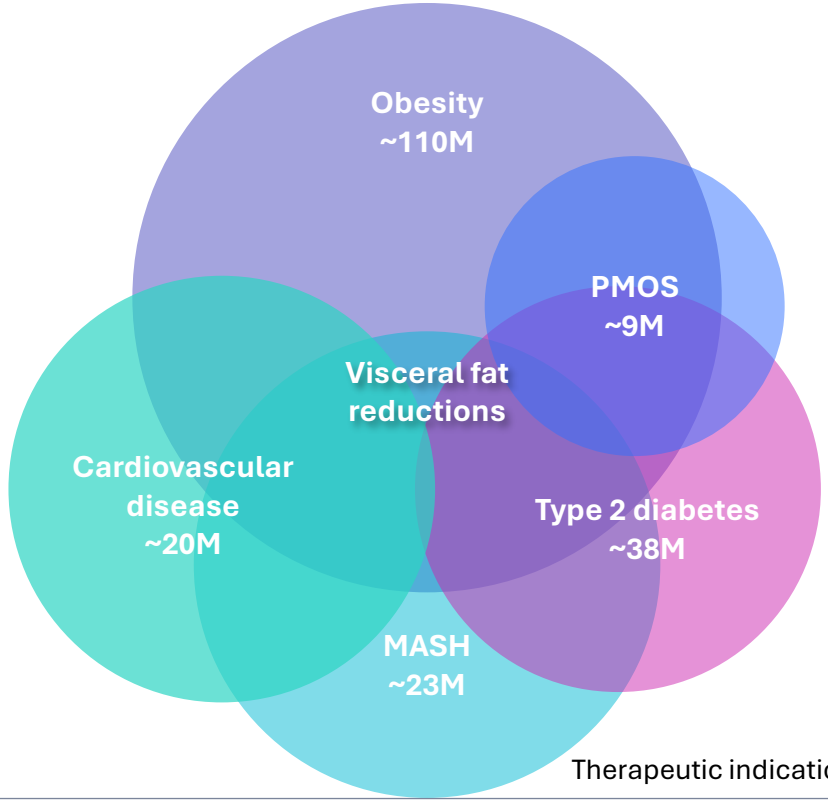
An off-ramp post-incretin treatments

- 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

PMOS: Polyendocrine Metabolic Ovarian 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

WVE-006 (investigational GalNAc-RNA editing AIMer) is a potentially transformative approach for both lung and liver manifestations of Pi*ZZ AATD

Significant unmet need in AATD

Current standard of care: Weekly IV augmentation is the only treatment for AATD lung disease

Augmentation limited by:

- ⊗ Weekly IV infusions
- ⊗ Does not address liver disease
- ⊗ Does not address root cause
- ⊗ Replaces protein, not production

Resulting in need for therapies that can:

- Address **root cause** of both **lung and liver disease**
- Restore **dynamic production** of **functional AAT** with a **safe, convenient** subcutaneous therapy

WVE-006

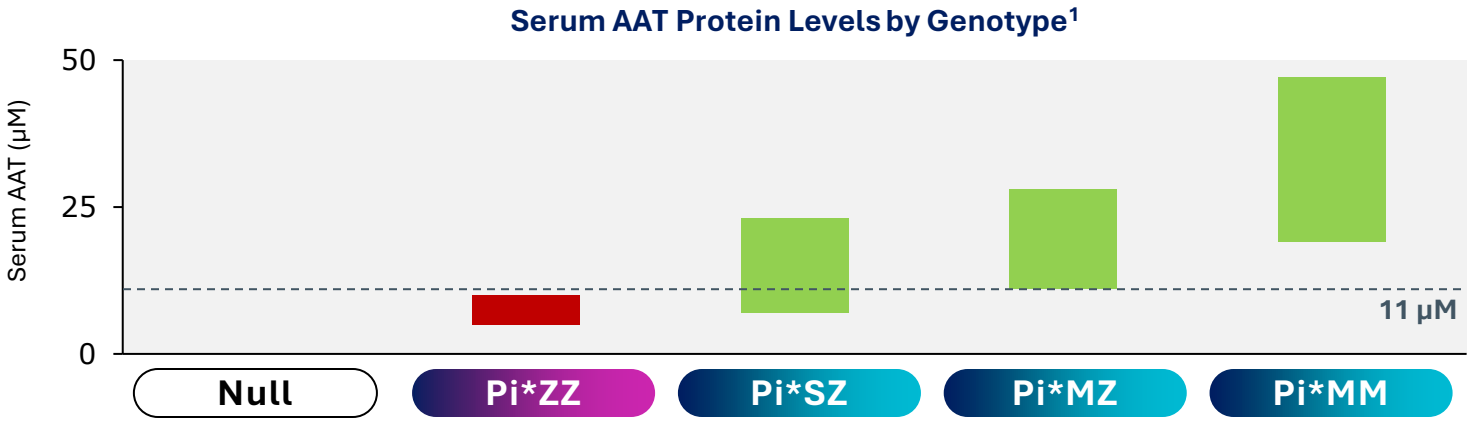
Focused on RNA editing to restore functional AAT, not augmentation

- ✓ **Restores wild-type M-AAT protein**
- ✓ **Reduces toxic Z-AAT protein**
- ✓ **Addresses both lung and liver disease**
- ✓ **Generally safe and well tolerated**

~200,000 people living with Pi*ZZ AATD across the US and Europe

1. Packer, et al. 2024, Methods and Compositions for Treating Alpha-1 Antitrypsin Deficiency, PCT/US2024/034189.

Treatment target: Heterozygous MZ genotype with M-AAT >50% AAT and a dynamic CRP response has low risk of liver and lung disease



Serum AAT composition	No AAT	100% Z-AAT	S-AAT and Z-AAT	Mean 64% M-AAT (range: 57%-71%)[2]	100% M-AAT
Risk of lung disease[3]	Very high	High	Low	Low	Normal
Risk of liver disease[3]	Normal	High	Low	Low	Normal
AAT levels increase with acute phase response[4]	N/A	No	Yes	Yes	Yes

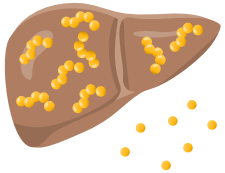
WAVE LIFE SCIENCES

1. Range of observed serum AAT levels from Bornhorst, et al. 2013 CHEST 143:1000-1008; 2. Percent M-AAT of total AAT from a natural history cohort of individuals with M/Z genotype using the same LC-MS/MS assay in RestorAATion-2; 3. Brode, et al. 2012 CMAJ 184:1365-1371; 4. Sanders, et al. 2018 COPD 15:10-16

RNA editing expected to deliver even greater impact over time with continued treatment and improved liver health

Pi*ZZ

Liver disease

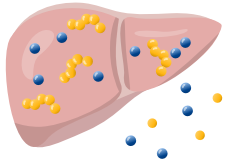


High Z-AAT aggregation and liver inflammation

WVE-006

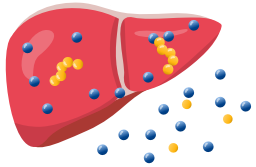
Pi*MZ-like

Reduce Z-AAT to prevent liver damage



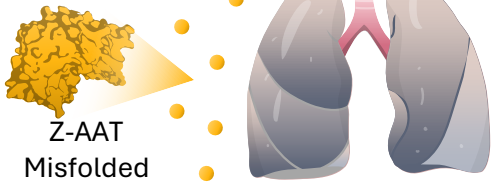
~50% M-AAT produced in liver

Z-aggregate clearance over time



Increasing hepatocyte health

Lung disease

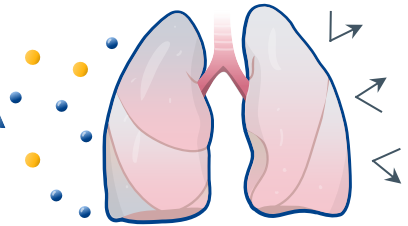


Z-AAT Misfolded Protein

100% Z-AAT, 0% M-AAT

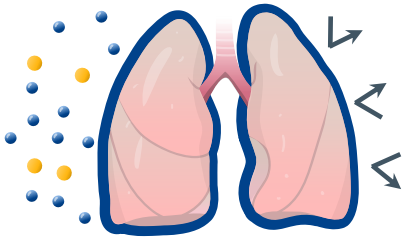
Wild-type M-AAT Protein

Restore M-AAT to prevent lung damage



>50% M-AAT

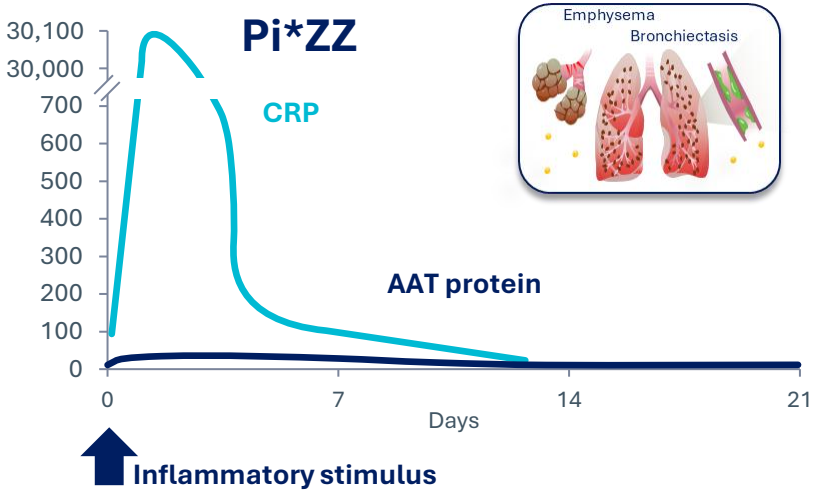
AAT levels responsive to CRP



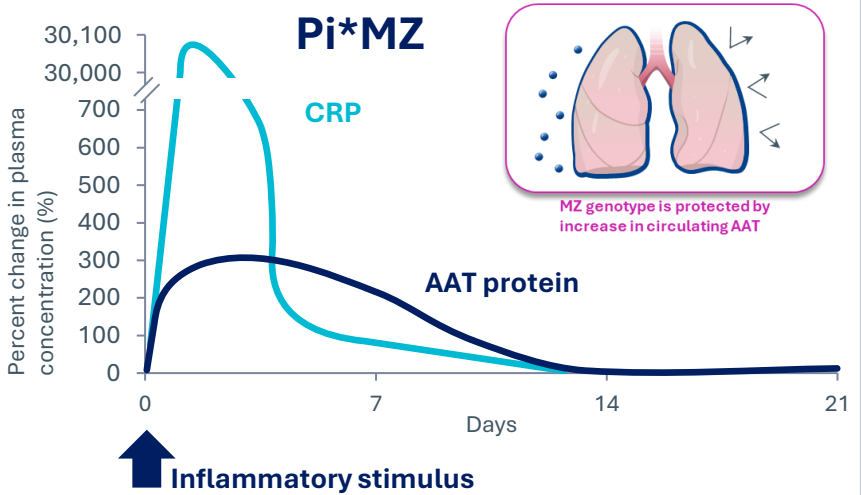
Potential for higher levels of serum AAT

Pi*ZZ individuals have an impaired serum AAT increase during acute-phase responses (APRs), when they need it most

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

WVE-006 restores dynamic production of AAT protein as part of APRs to protect lungs from damage

APRs require a rapid rise in AAT levels to prevent lung damage

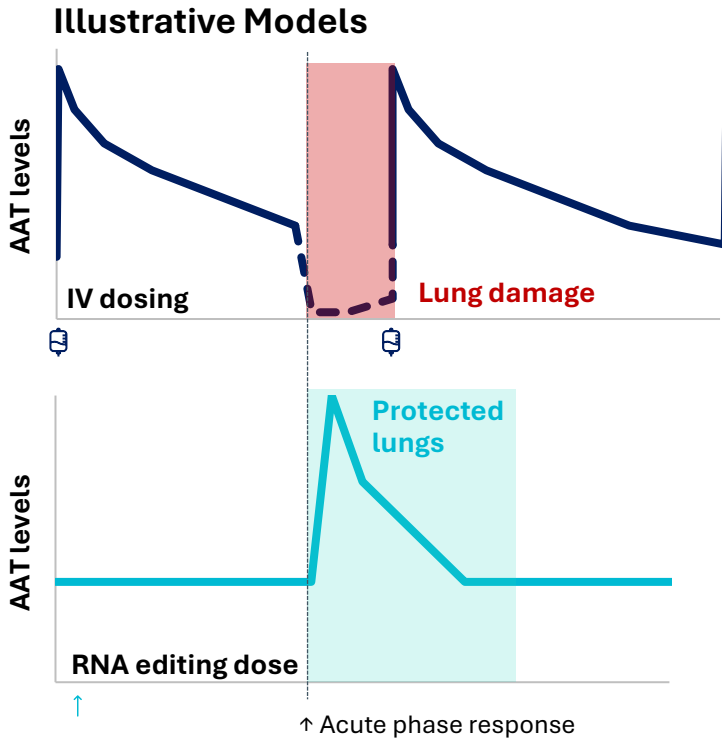
- Even with augmentation therapy, in ZZ individuals, exacerbations occur on average 1–2x yearly
- These exacerbations could deplete AAT levels within hours[1]
- In healthy (including MZ) individuals, AAT levels rise quickly (24–72 hours) after stimulus

Standard of care (augmentation therapy) may leave patients at risk

- Exogenous AAT levels risk **depletion** before next scheduled IV dose

WVE-006 treatment response is dynamic

- Endogenous AAT levels increase during acute phase response



Right: Illustrative model of impact of acute phase response

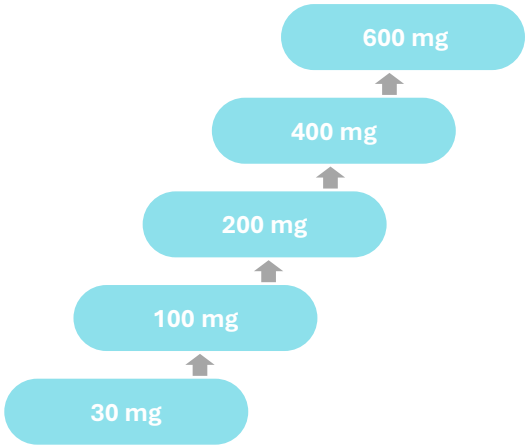
1. Liou & Campbell, *Journal of Immunology* 1996; Thulborn et al., *Respiratory Research* 2019; Beatty et al., *Journal of Biological Chemistry* 1980.

RestorAATion-2 trial ongoing in individuals living with Pi*ZZ AATD

RESTORAATION

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

SAD → MAD Multi-dosing complete



SAD	MAD
600 mg Single dose	600 mg x 4 doses Monthly
400 mg Single dose	400 mg x 4 doses Monthly
200 mg Single dose	200 mg x 7 doses Biweekly

Study key objectives

Safety and tolerability	Pharmacokinetics	Serum M-AAT levels

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

Treatment with WVE-006 achieved Pi*MZ-like profile across doses: delivering potential liver and lung benefits with a safe and convenient therapy

		Protecting the liver	Protecting the lung	
WVE-006	**Total AAT**	**Reduce Z-AAT**	**Generate healthy, wild-type M-AAT**	**MZ-like dynamic AAT production**
200 mg biweekly	**11.9** µM	**71%** reduction	**64%** M-AAT of total AAT	**Three** acute phase responses (up to **>20 µM** total AAT)
400 mg monthly	**13.6** µM	**68%** reduction	**59%** M-AAT of total AAT	CRP increases correlated with AAT increases

Safe and convenient

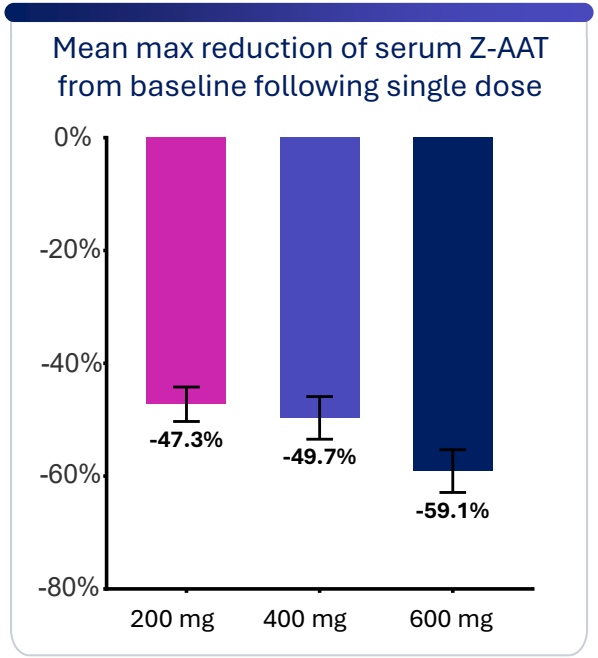
- Generally safe and well tolerated
- Subcutaneous delivery, with potential for self-administration
- Potential for monthly dosing

Data from 600 mg monthly dose cohort expected in 2H 2026

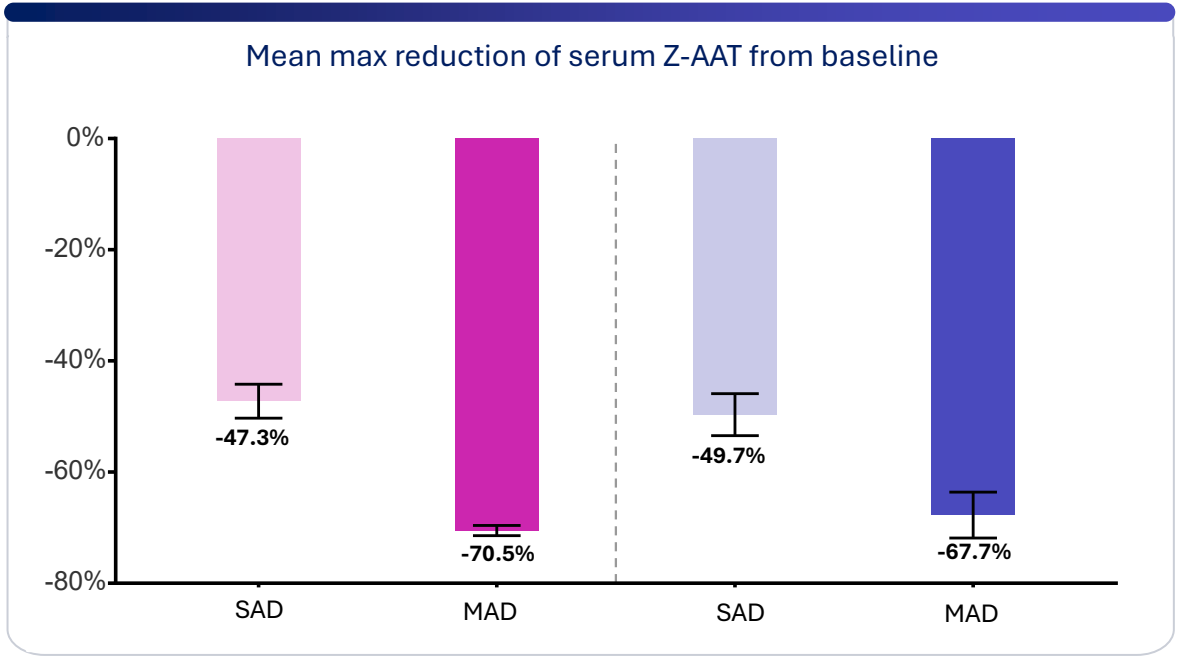
Circulating M-AAT, Z-AAT, and total (M + Z) AAT protein in the serum were measured by highly selective and sensitive LC-MS/MS assays (LLOQ: 0.096 µM (M), 0.029 µM (Z)) and reported as mean participant MAD maximums. In a natural history cohort of individuals with M/Z genotype using the same LC-MS/MS assay in RestorAATion-2, M-AAT% of total AAT mean was 64% (range 57%-71%).

Up to 71% reduction in circulating, mutant Z-AAT supporting potential improvement in liver health

SAD cohorts: Dose-dependent Z-AAT reductions



MAD cohorts: Similar reductions with extended dosing interval

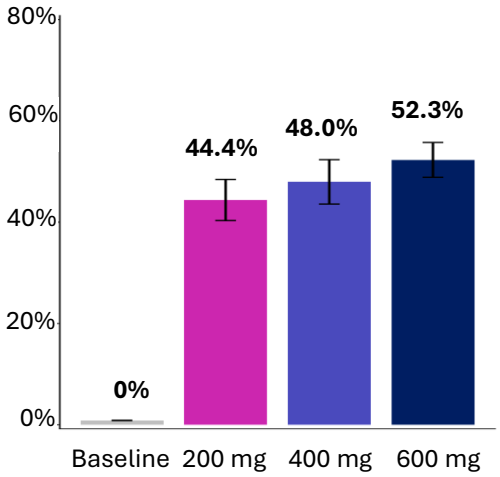


Error bars represent the standard error of the mean (SE).

WVE-006 generated circulating wild-type M-AAT within the MZ range (up to 64%) with no bystander edits, supporting potential improvement in lung health

SAD cohorts: Dose-dependent M-AAT restoration

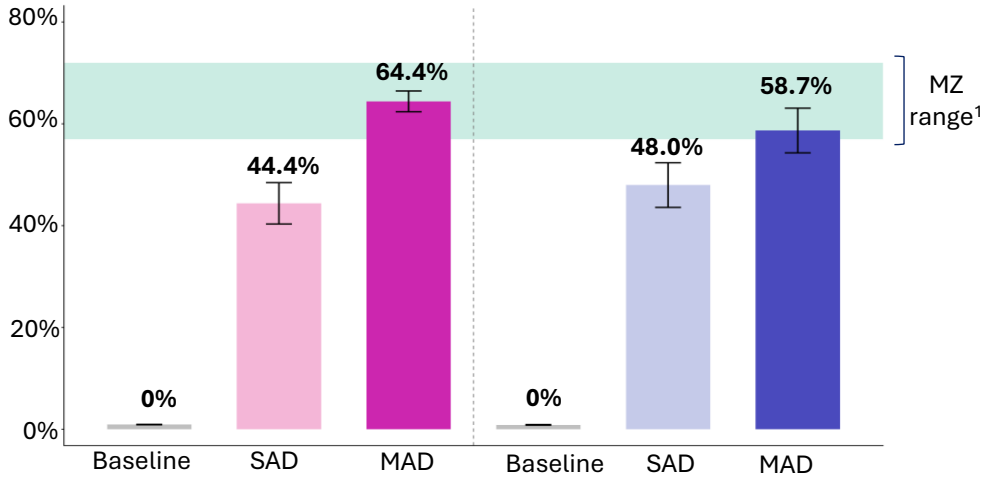
Mean max M-AAT (% of total AAT) following a single dose



MAD cohorts: Similar M-AAT% with extended dosing interval

Biweekly (200 mg x 7 doses) Monthly (400 mg x 4 doses)

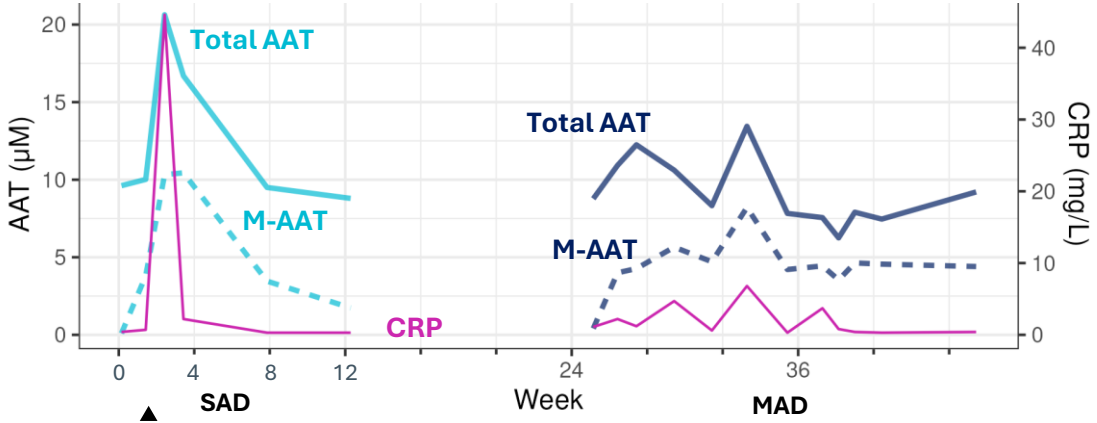
Mean max M-AAT (% of total AAT)



1. In a natural history cohort of individuals with M/Z genotype using the same LC-MS/MS assay in RestorAATion-2, M-AAT% of total AAT mean was 64% (range 57%-71%). At baseline, serum M-AAT values were below the LLOQ (0.096 µM); the LLOQ value was used for baseline calculations. Error bars represent the standard error of the mean (SE).

WVE-006 continues to demonstrate dynamic increases of AAT during acute phase responses

Total AAT reached 20.6 µM two weeks post single 200 mg dose during acute phase response



▲ Acute phase response due to a kidney stone

CRP levels are correlated with AAT elevations across RestorAATion-2

- Two additional acute phase responses (URI-common cold) accompanied by 57.8% and 59.8% increases in AAT from pre-event[1]
- CRP increases are strongly correlated with AAT increases (r=0.73, p<0.001, n=19) [2,3]

Across RestorAATion-2 even low elevations in CRP are associated with increased production of AAT

CRP: C-reactive protein; URI: upper respiratory infection
1 – The most recent non-missing assessment obtained prior to the first observation where CRP exceeded the upper limit of normal (ULN);
2 –Pearson correlation of log-transformed fold changes from pre-event (p < 0.001);
3 – N=19 defined as transitions from normal (≤ ULN) to elevated (> ULN) CRP

WVE-006 offers a differentiated treatment approach for AATD compared to current standard of care and other therapies in clinical development

	Protecting the liver	Protecting the lung		Safe and convenient	
	Reduce Z-AAT	Enable dynamic AAT production	Provide healthy, wild-type M-AAT	Infrequent SC dosing	Safe & well-tolerated
WVE-006 *(investigational)*	✓	✓	**100% wild-type M-AAT**	**SC, Q4W**	✓
Approved augmentation therapy[1]	✗	✗	100% wild-type M-AAT	IV, weekly	✓
Recombinant augmentation therapy[2] *(investigational)*	✗	✗	100% Fc-dimerized AAT	IV, Q3-4W	✓
DNA base editing *(investigational)*	✓	✓	Less than 50% wild-type M-AAT[4]	IV, single dose (uncertain durability, redosing may not be possible)	Liver enzyme elevations[3]; Requires LNPs; Risk of permanent off-target effects, including in cancer-associated genes[5]
AAT siRNA[6] *(investigational)*	✓	✗	✗	SC, Q3M	Potential exacerbation of lung disease due to AAT knockdown[6]

WAVE LIFE SCIENCES

SC: subcutaneous; IV: intravenous. 1. Prolastin label; 2. Barjaktarevic, et al. Efdoralprin Alfa vs. Plasma-derived Alpha-1 Proteinase Inhibitor (pdA1PI) Augmentation Therapy in Adults With Alpha-1 Antitrypsin Deficiency (AATD) Emphysema: Results From Phase 2 ElevAATe Trial [Conference abstract] ATS 2026; 3. BEAM-302 Topline Data Update, March 25, 2026; 4. Banerjee, et al. BEAM-302 decreases hepatic aggregates of mutant AAT and increases circulating functional AAT in rodent models of Alpha-1 Antitrypsin Deficiency [Poster] 2023 ESGCT Congress; 5. Packer, et al. (2024) Methods and Compositions for Treating Alpha-1 Antitrypsin Deficiency (International Patent Application PCT/US2024/034189). https://patentimages.storage.googleapis.com/f7/f0/9a/f88f452755cb16/WO2024259364A2.pdf ; 6. Strnad, et al. 2022 N Engl J Med 387:514-524.

WVE-006 aims to support a differentiated value proposition for Pi*ZZ individuals, HCPs, and payers

Reduce Z-AAT to prevent liver disease

Provide healthy, wild-type M-AAT to protect lung

Enable dynamic AAT production during acute phase response

WVE-006 for AATD

Infrequent subcutaneous dosing; potential for self-administration

Generally safe and well tolerated

No bystander edits or other permanent DNA modifications

Expect to meet with the FDA on a potential accelerated approval pathway end of summer 2026

WVE-008
RNA editing (AIMer)

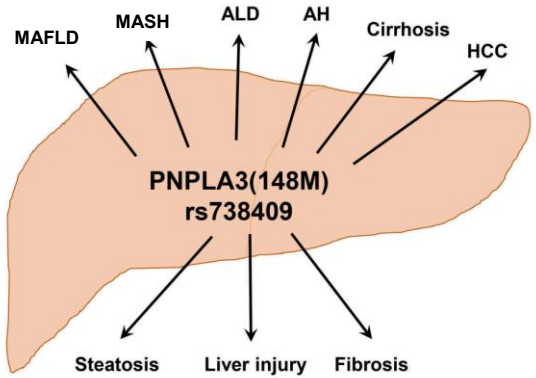
PNPLA3 I148M liver disease

WAVE LIFE SCIENCES

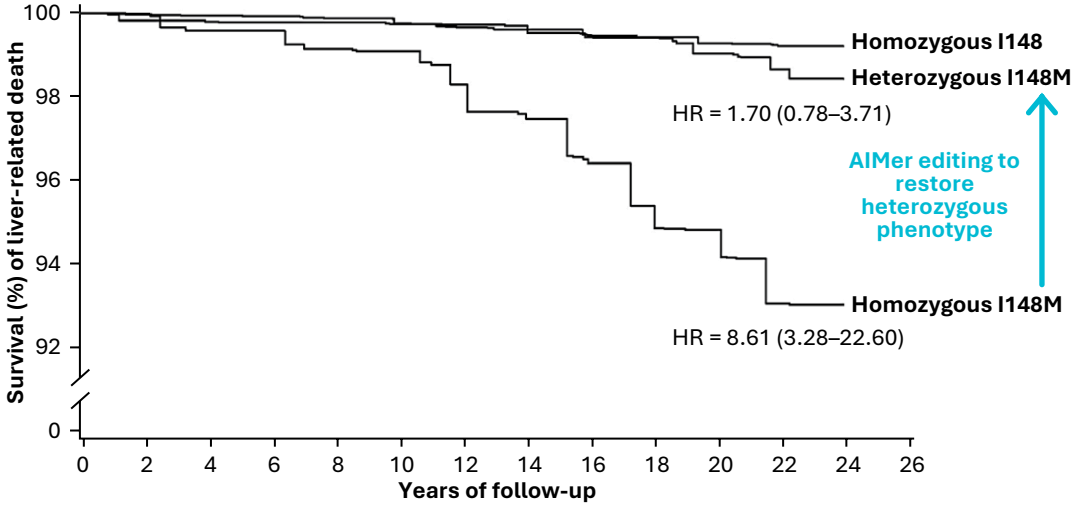
WVE-008 for PNPLA3 I148M liver disease

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



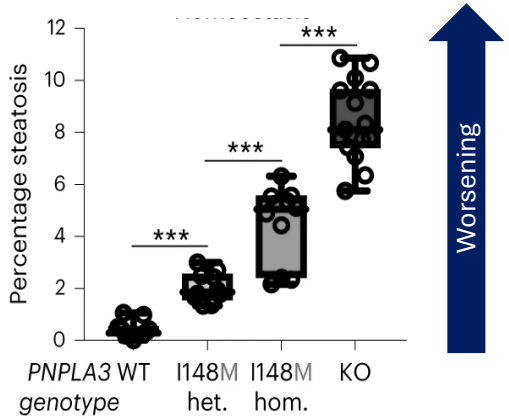
Over nine million homozygous PNPLA3 I148M individuals with genetic liver disease in US and Europe

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

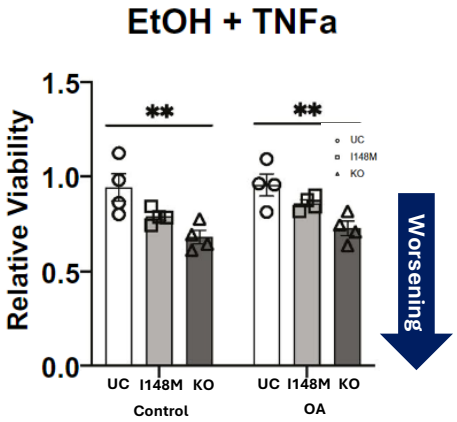
MAFLD, Metabolic dysfunction-associated fatty liver disease; MASH, Metabolic dysfunction-associated steatohepatitis; ALD, alcoholic liver disease; AH, Alcohol-associated hepatitis; HCC, hepatocellular carcinoma

Silencing of PNPLA3 in normal liver may worsen basal physiological functions

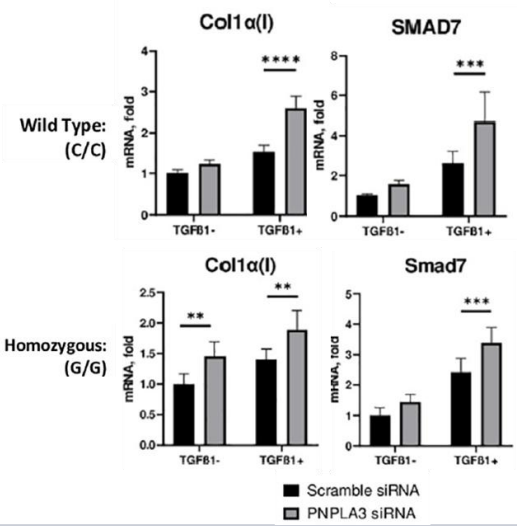
Silencing PNPLA3 worsens steatosis in iPSC-derived human liver organoids[2]



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



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



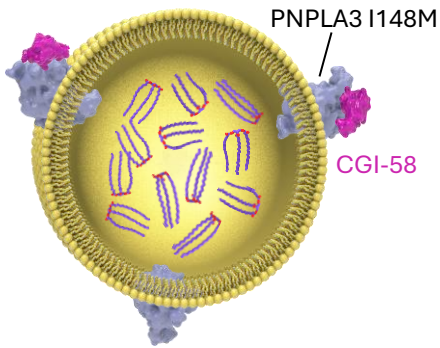
Functional PNPLA3 is imperative for liver health beyond improvements in steatosis

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

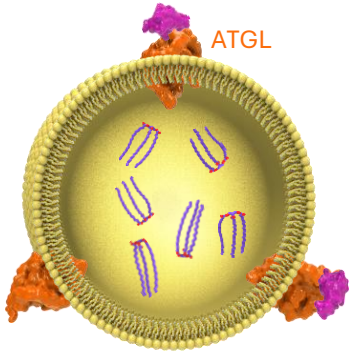
RNA editing approach

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



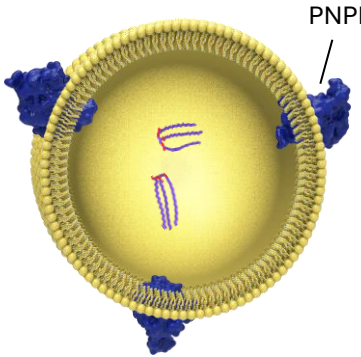
- PNPLA3 I148M accumulates on LDs, sequesters CGI-58, inhibits ATGL's lipase activity and lipid mobilization from ER
- Suppresses retinol metabolism in liver and worsens inflammation and fibrosis
- Promotes liver fat accumulation and fibrosis through activation of stellate cells

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



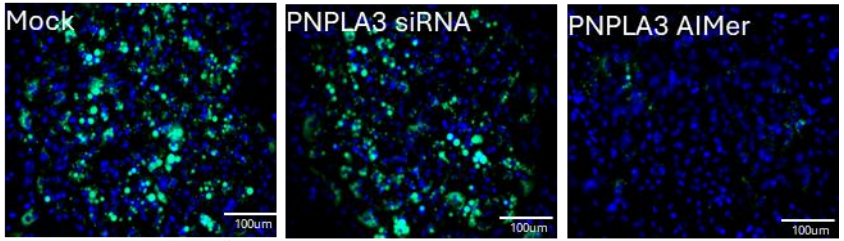
- Restores full PNPLA3 activity
- **Restores lipid mobilization, reverses steatosis, fibrosis, ballooning, and inflammation**

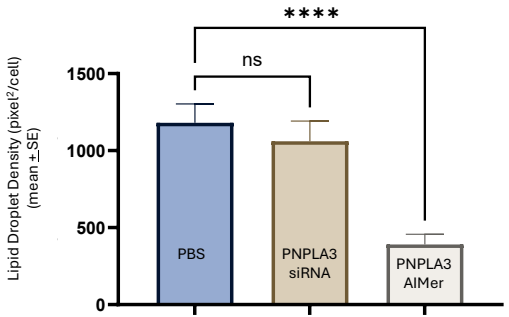
ATGL: adipose triglyceride lipase; CGI-58: co-factor for ATGL; ER endoplasmic reticulum; LDs: lipid droplets; CGI-58 also called ABHD5

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

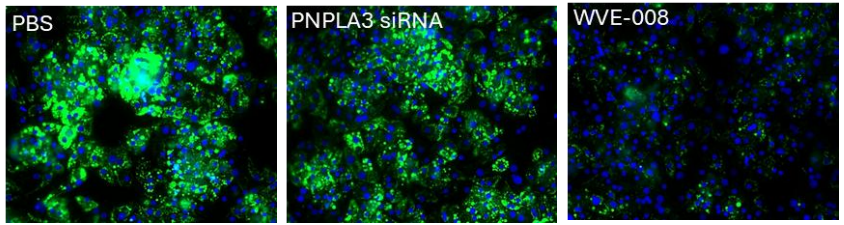
AIMers achieve efficient editing of PNPLA3, leading to reduction of liver fat

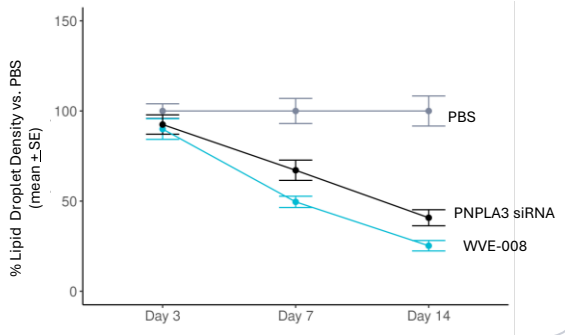
Significant decrease in liver fat with PNPLA3 editing in human HEPATOPAC® model with homozygous I148M





Decrease in liver fat with WVE-008 in monolayer model

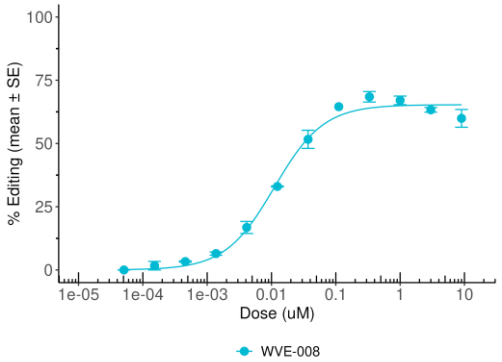




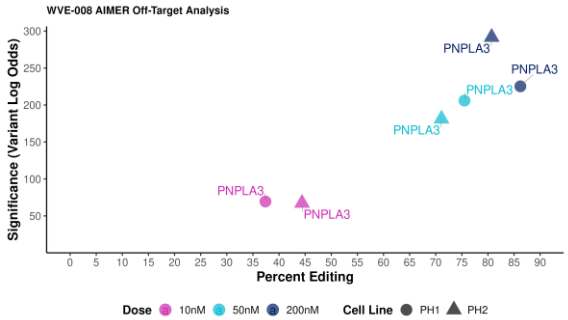
One-way ANOVA with Dunnett post hoc test comparisons to Mock **** P< 0.0001

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

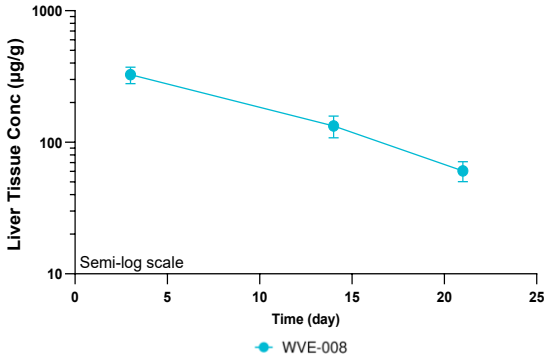
Potential editing with WVE-008



Highly specific editing with WVE-008



Tissue exposure supports excellent delivery



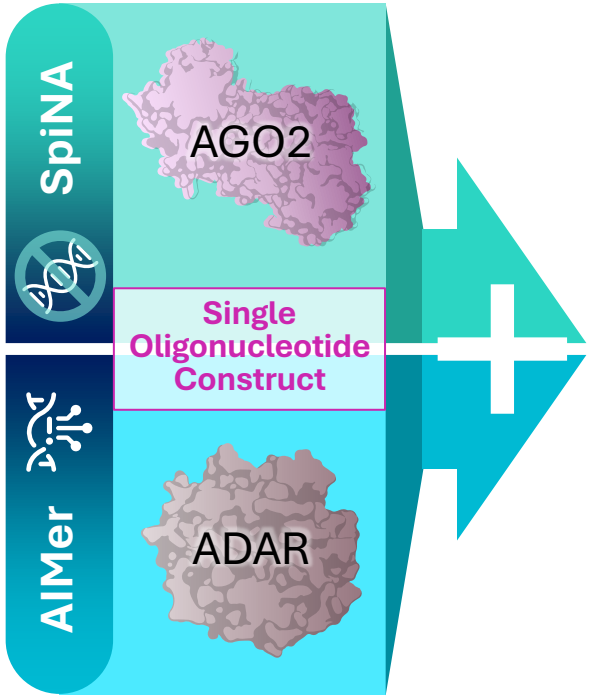
Expect to file Clinical Trial Application (CTA) for WVE-008 in 2H 2026

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.

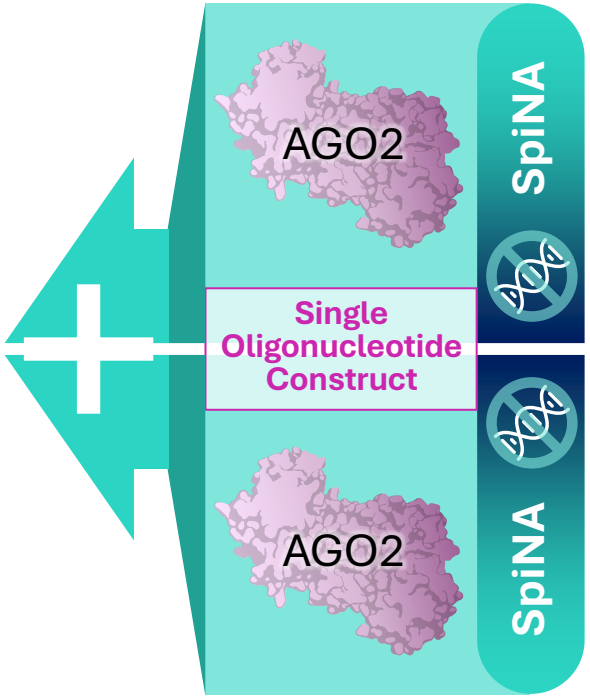
Reimagining RNA medicines

WAVE® LIFE SCIENCES

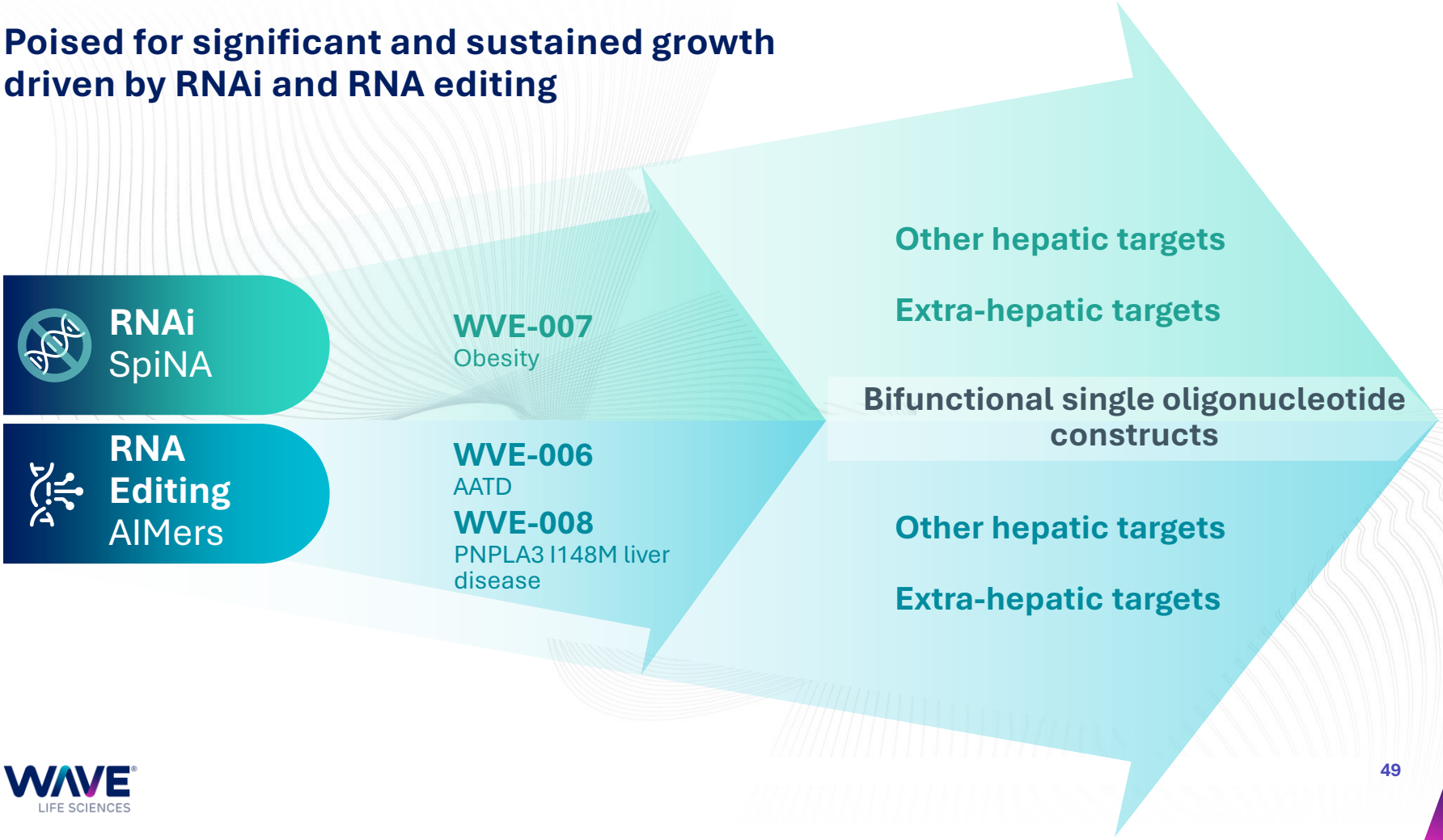
Reimagining RNA medicines: Bifunctional modalities



- ✓ 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



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



WAVE® LIFE SCIENCES

Reimagine possible.

For questions contact:
investorrelations@wavelifesci.com