UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 30, 2026

WAVE LIFE SCIENCES LTD.
(Exact name of registrant as specified in its charter)

Singapore	**001-37627**	**98-1356880**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

7 Straits View #12-00, Marina One East Tower	
Singapore	**018936**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: +65 6236 3388

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading symbol**	**Name of each exchange on which registered**
$0 Par Value Ordinary Shares	WVE	The Nasdaq Global Market

Item 2.02 Results of Operations and Financial Condition.

On July 30, 2026, Wave Life Sciences Ltd. (the "Company") announced its financial results for the quarter ended June 30, 2026. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 7.01 Regulation FD Disclosure.

From time to time, the Company presents and/or distributes slides and presentations to the investment community to provide updates and summaries of its business. On July 30, 2026, the Company updated its corporate presentation, which is available on the "Investors" section of the Company's website at http://ir.wavelifesciences.com/. This presentation is also furnished as Exhibit 99.2 to this Current Report on Form 8-K

The information in these Items 2.02 and 7.01 are being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall they be deemed incorporated by reference into any registration statement or other filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following exhibits relating to Items 2.02 and 7.01 are furnished and not filed:

Exhibit No.	**Description**
99.1	Press Release issued by Wave Life Sciences Ltd. dated July 30, 2026
99.2	Corporate Presentation of Wave Life Sciences Ltd. dated July 30, 2026
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

WAVE LIFE SCIENCES LTD.

By: */s/ Kyle Moran, CFA*
Kyle Moran, CFA
Chief Financial Officer

Date: July 30, 2026

Wave Life Sciences Reports Second Quarter 2026 Financial Results and Provides Business Update

Dosing underway in Phase 2a multidose portion of the INLIGHT™ trial of WVE-007 (INHBE GalNAc-siRNA) in individuals with obesity (BMI: 35-50 kg/m²) and comorbidities; trial will also inform WVE-007's potential in MASH, type 2 diabetes, and other cardiometabolic diseases

Phase 2 combination with incretin and post-incretin maintenance trials of WVE-007 on track to initiate in 2H 2026

FDA meeting scheduled for end of summer 2026 on potential accelerated approval pathway for WVE-006 (GalNAc-RNA editing); data from RestorAATion-2 trial support differentiated therapeutic approach for both lung and liver manifestations of AATD

CTA submission for WVE-008 for PNPLA3 liver disease (GalNAc-RNA editing) on track for 2H 2026

Well capitalized with cash, cash equivalents, and marketable securities of $490.6 million as of June 30, 2026 and expected cash runway into 3Q 2028

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

CAMBRIDGE, Mass., July 30, 2026 – Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health, today announced financial results for the second quarter ended June 30, 2026, and provided a business update.

"Our second quarter performance reflects disciplined execution across the pipeline," said Paul Bolno, MD, MBA, President and Chief Executive Officer at Wave Life Sciences. "We recently initiated dosing in the Phase 2a portion of our INLIGHT trial in obesity. Our Phase 1 clinical data have already demonstrated substantial reductions of fat – particularly harmful visceral fat – without muscle loss, and with the potential for once or twice-yearly dosing. We expect the Phase 2a portion of the INLIGHT trial, in individuals with higher BMI and higher body fat, to demonstrate WVE-007's broad potential to deliver even greater fat loss and improvements in body composition, as well as benefits across additional cardiometabolic biomarkers such as liver fat. In tandem with this progress, we are working expeditiously to initiate Phase 2 trials evaluating WVE-007 in combination with incretins and as post-incretin maintenance; we believe WVE-007 has the potential to transform the current obesity treatment landscape."

Dr. Bolno added, "In RNA editing, our RestorAATion-2 clinical data support WVE-006's potential to offer a new standard of care for individuals living with AATD by treating both lung and liver manifestations of the disease, and restoring dynamic response of AAT protein, with convenient, infrequent subcutaneous dosing, and without the risks associated with DNA editing. We look forward to meeting with the FDA to discuss a pathway for accelerated approval for WVE-006. Building on our clinical success in RNA editing, WVE-008, our PNPLA3 RNA editing program, has the potential to address the nine million individuals living with this genetic liver disease. It's exciting to see the clinical translation of our RNAi and RNA editing programs, enabled by our unique and proprietary chemistry, and supported by human genetics. We expect to provide further updates on our pipeline and platform innovations at our annual investor day this fall."

Recent Business Highlights and Expected Milestones

Obesity

- **WVE-007** is an investigational GalNAc-siRNA (SpiNA) designed to induce fat loss without muscle loss. With strong evidence from human genetics, silencing INHBE mRNA is a promising therapeutic strategy to treat obesity, distinct from incretin-based approaches. WVE-007 is being evaluated in the ongoing placebo-controlled INLIGHT clinical trial.
- **Phase 1 INLIGHT trial:** The ongoing, single dose portion is evaluating otherwise healthy individuals with less fat and lower BMI (average ~32 kg/m^2) than Phase 2 and 3 obesity trials. Data from the INLIGHT trial have demonstrated total body fat reduction, with muscle preservation, as well as clinically meaningful reductions in visceral fat[1] and waist circumference. WVE-007 continued to be generally safe and well tolerated and data support potential for once or twice-yearly dosing. Additional data from the INLIGHT trial, including data from the 600 mg Phase 1 SAD cohort, are expected in the second half of 2026.
- **Phase 2a INLIGHT trial:** Dosing is underway in the Phase 2a multidose portion of the INLIGHT trial of WVE-007 in individuals with higher BMI (35-50 kg/m^2), with and without type 2 diabetes. This portion of the INLIGHT trial is evaluating participants with greater adiposity, consistent with Phase 2 and 3 obesity trials. This portion of the trial is enrolling participants across the U.S. and Europe and includes multiple assessments over a 12-month period, including body weight, waist circumference, body composition (MRI and DEXA), liver fat (MRI-PDFF), HbA1c, and lipid levels. These data will inform further development of WVE-007 in obesity, as well as in MASH, type 2 diabetes, and other cardiometabolic diseases.
- **Combination with incretin and post-incretin maintenance:** Wave expects to initiate Phase 2 trials of WVE-007 in the combination and maintenance settings in the second half of 2026.

Alpha-1 antitrypsin deficiency (AATD)

- **WVE-006** is an investigational GalNAc-conjugated, subcutaneously delivered, RNA editing oligonucleotide (AIMer) for AATD. WVE-006 is being evaluated in the ongoing Phase 1b/2a RestorAATion-2 open-label clinical trial in individuals with AATD who have the homozygous Pi*ZZ mutation.
- **RestorAATion-2 trial:** The 200 mg, 400 mg, and 600 mg cohorts are fully enrolled and dosing is complete.
- In May 2026, the company shared clinical data from the 200 mg (single and biweekly), 400 mg (single and monthly), and 600 mg (single dose) cohorts of the ongoing RestorAATion-2 clinical trial that demonstrated WVE-006 achieved key AATD treatment goals by recapitulating an MZ-like phenotype, including robust, dose-dependent reductions of circulating, mutant Z-AAT protein, with corresponding increases in wild-type M-AAT protein, and restoration of dynamic AAT response. Wave expects to share data from the 600 mg (monthly) multidose cohort in the second half of 2026.
- Wave's request for a meeting regarding a potential accelerated approval pathway for WVE-006 was granted by the U.S. Food and Drug Administration (FDA). The meeting is scheduled for the end of summer 2026.

PNPLA3 I148M liver disease

- **WVE-008:** Wave is building on its clinical success in RNA editing by advancing WVE-008, a GalNAc-conjugated AIMer for homozygous PNPLA3 I148M liver disease. There is a growing body of clinical evidence supporting RNA editing as a preferred therapeutic strategy over silencing.

- In May 2026, Wave shared preclinical data supporting WVE-008 in a poster presentation at the European Association for the Study of the Liver (EASL) Congress. These data demonstrated that Wave's PNPLA3 AIMers delivered substantial editing of the PNPLA3 I148M transcript, exceeding the ~50% threshold expected to lower risk for liver disease.
- A clinical trial application (CTA) filing for WVE-008 is on track for the second half of 2026.

Other pipeline programs (HD and DMD)

- Wave continues partnering discussions for WVE-003 (Huntington's disease) and WVE-N531 (Duchenne muscular dystrophy, exon 53). With respect to WVE-N531, Wave is evaluating the evolving regulatory and commercial landscape in DMD and exploring potential partnerships in advance of filing a New Drug Application (NDA).

Emerging pipeline

- **Investor Day 2026:** Wave plans to host an investor day in the fall of 2026, where the company expects to share updates from its clinical and preclinical pipeline of RNA medicines.

Financial Highlights

- Cash, cash equivalents, and marketable securities were $490.6 million as of June 30, 2026, compared to $602.1 million as of December 31, 2025. Wave expects that its current cash, cash equivalents, and marketable securities will be sufficient to fund operations into the third quarter of 2028. Potential future milestone and other payments to Wave under its GSK collaboration are not included in its cash runway.
- Revenue recognized was $2.3 million for the second quarter of 2026 as compared to $8.7 million in the prior year quarter.
- Research and development expenses were $51.3 million in the second quarter of 2026 as compared to $43.5 million in the same period in 2025.
- General and administrative expenses were $24.8 million in the second quarter of 2026 as compared to $18.0 million in the same period in 2025.
- Net loss was $69.4 million for the second quarter of 2026 as compared to a net loss of $50.5 million in the prior year quarter.

Investor Conference Call and Webcast

Wave will host an investor conference call today at 8:30 a.m. ET to review the second quarter 2026 financial results and pipeline updates. A webcast of the conference call can be accessed by visiting "Investor Events" on the investor relations section of the Wave Life Sciences website: https://ir.wavelifesciences.com/events-publications/events. Analysts planning to participate during the Q&A portion of the live call can join the conference call at the audio-conferencing link **here**. Following the live event, an archived version of the webcast will be available on the Wave Life Sciences website.

About Wave Life Sciences

Wave Life Sciences (Nasdaq: WVE) is a biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health. Wave's PRISM® platform combines multiple modalities, chemistry innovation, and deep insights in human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Its toolkit of RNA-targeting modalities, including RNAi (SpiNA) and RNA editing (AIMers), provides Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's pipeline is focused on its obesity (WVE-007), alpha-1 antitrypsin deficiency (WVE-006) and PNPLA3 I148M liver disease (WVE-008) programs, and also includes clinical programs in Duchenne muscular dystrophy and Huntington's disease, as well as several preclinical programs utilizing the company's versatile RNA medicines platform. Driven by the calling to "Reimagine Possible," Wave is leading the charge toward a world in which human potential is no longer hindered by the burden of disease. Wave is headquartered in Cambridge, MA. For more information on Wave's science, pipeline and people, please visit www.wavelifesciences.com and follow Wave on X and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, concerning our goals, beliefs, expectations, strategies, objectives and plans, and other statements that are not necessarily based on historical facts, including statements regarding the following, among others: the anticipated initiation, timing, design, progress, data and announcements related to our clinical trials, including interactions with and feedback from regulators and any potential registrational submissions based on these data; the future performance and results of our programs in clinical trials, including the anticipated therapeutic benefits of such programs, and our expectations with respect to how our clinical data may predict success for our future therapeutic candidates and data readouts; the potential commercialization of our programs the potential size of the markets that our therapeutics may address; preclinical activities and programs and their potential to transition into clinical-stage programs, and the timing, progress and announcement of such events; the progress and potential benefits, including the potential achievement of milestones, of collaborations and strategic partnerships; the expected benefits of our stereopure oligonucleotides compared with stereorandom oligonucleotides; the breadth and versatility of our PRISM® drug discovery and development platform; the potential benefits of our RNA-targeting modalities, including RNAi (SpiNA), and RNA editing (AIMers); the potential for certain of our programs to be best-in-class or first-in-class, or to change the existing treatment paradigm or show substantial benefits over existing standards of care; our financial performance, including the anticipated duration of our cash runway and our ability to fund future operations; our intended uses of capital; and our expectations regarding the impact of any potential global macro events on our business. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual results to differ materially from those indicated by these forward-looking statements as a result of these risks, uncertainties and important factors, including, without limitation, the clinical results and timing of our programs, which may not support further development of our product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing current and future clinical trials and regulatory processes; the continued development and acceptance of nucleic acid therapeutics as a class of drugs; our ability to demonstrate the therapeutic benefits of our stereopure candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our ability to obtain, maintain and

protect intellectual property; our ability to fund our operations and to raise additional capital as needed; competition from others developing therapies for similar uses; and any impacts on our business as a result of or related to any global economic uncertainty or market disruptions, as well as the other risks and uncertainties described in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as amended, and in other filings we make with the SEC from time to time. In addition, any forward-looking statements represent our views only as of today and should not be relied upon as representing our views as of any subsequent date. We undertake no obligation, except to the extent required by law, to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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[1] Gabriely et al., Diabetes 2002; Campos et al., Diabetes & Vascular Disease Research 2019; Huang et al., Front Endocrinol 2023.; Cesaro et al., Front Cardiovasc Med 2023; Khawaja et, al., Curr Cardiol Rep 2024; Hiuge-Shimizu et al., J Atheroscler Thromb 2011.; Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020; Hanlon & Yuan, Clin Liver Dis 2021.; Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	June 30, 2026	December 31, 2025
Assets		
Current assets:		
Cash and cash equivalents	$ 368,008	$ 602,068
Marketable Securities	122,594	—
Accounts receivable	888	1,276
Prepaid expenses	12,121	8,395
Other current assets	3,897	3,075
Total current assets	507,508	614,814
Long-term assets:		
Property and equipment, net of accumulated depreciation of $50,819 and $49,522 as of June 30, 2026 and December 31, 2025, respectively	6,833	7,405
Operating lease right-of-use assets	39,498	12,458
Restricted cash	3,815	3,806
Other assets	667	16
Total long-term assets	50,813	23,685
Total assets	$ 558,321	$ 638,499
Liabilities, Series A preferred shares, and shareholders' equity		
Current liabilities:		
Accounts payable	$ 20,362	$ 15,700
Accrued expenses and other current liabilities	18,242	26,564
Current portion of deferred revenue	8,703	44,440
Current portion of operating lease liability	3,508	8,361
Total current liabilities	50,815	95,065
Long-term liabilities:		
Deferred revenue, net of current portion	13,904	7,798
Operating lease liability, net of current portion	40,082	9,405
Total long-term liabilities	53,986	17,203
Total liabilities	$ 104,801	$ 112,268
Series A preferred shares, no par value; nil and 3,901,348 shares issued and outstanding at June 30, 2026 and December 31, 2025, respectively	$ —	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 193,277,622 and 187,660,263 shares issued and outstanding at June 30, 2026 and December 31, 2025, respectively	$ 1,627,209	$ 1,616,478
Additional paid-in capital	248,161	228,365
Accumulated other comprehensive loss	(172)	(250)
Accumulated deficit	(1,421,678)	(1,326,236)
Total shareholders' equity	$ 453,520	$ 518,357
Total liabilities, Series A preferred shares, and shareholders' equity	$ 558,321	$ 638,499

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2026	2025	2026	2025
Revenue	$ 2,272	$ 8,699	$ 40,518	$ 17,874
Operating expenses:				
Research and development	51,293	43,469	98,733	84,091
General and administrative	24,781	17,989	46,884	36,346
Total operating expenses	76,074	61,458	145,617	120,437
Loss from operations	(73,802)	(52,759)	(105,099)	(102,563)
Other income, net:				
Interest income	4,722	2,372	10,013	5,247
Other expense	(275)	(82)	(356)	(31)
Total other income, net	4,447	2,290	9,657	5,216
Loss before income taxes	(69,355)	(50,469)	(95,442)	(97,347)
Income tax benefit	—	—	—	—
Net loss	$ (69,355)	$ (50,469)	$ (95,442)	$ (97,347)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.34)	$ (0.31)	$ (0.47)	$ (0.60)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	204,008,712	163,987,640	202,098,901	163,266,106
Other comprehensive loss:				
Net loss	$ (69,355)	$ (50,469)	$ (95,442)	$ (97,347)
Foreign currency translation gain	123	43	119	101
Unrealized loss on marketable securities	(41)	—	(41)	—
Comprehensive loss	$ (69,273)	$ (50,426)	$ (95,364)	$ (97,246)

Exhibit 99.2



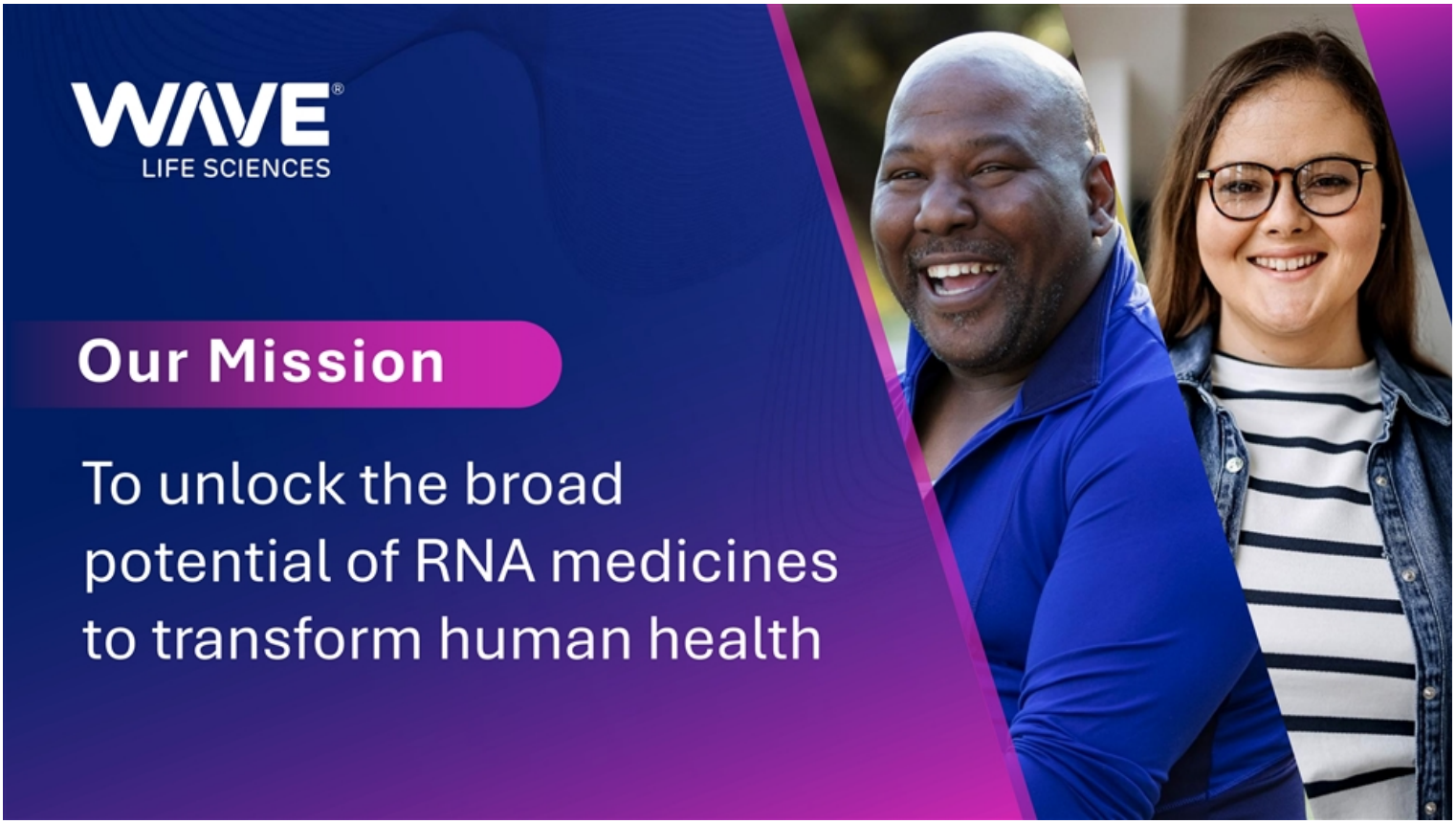
Wave Life Sciences

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

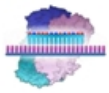
Differentiated RNA medicines platform and chemistry

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

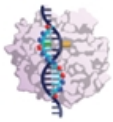
RNAi



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**

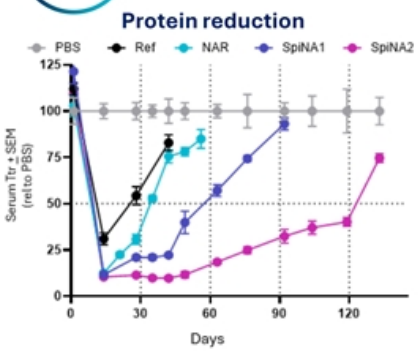
Unlocking emerging pipeline

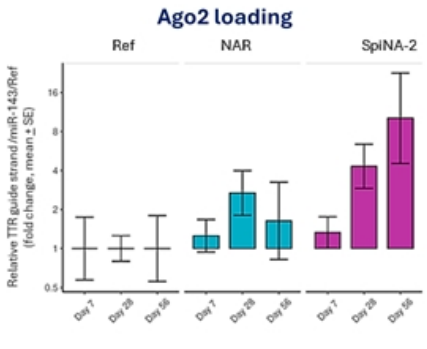
- **Extra-hepatic capabilities:** with RNAi and RNA editing
- **Bifunctional modalities:** single oligonucleotide constructs for dual RNAi silencing or RNAi silencing + RNA editing

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

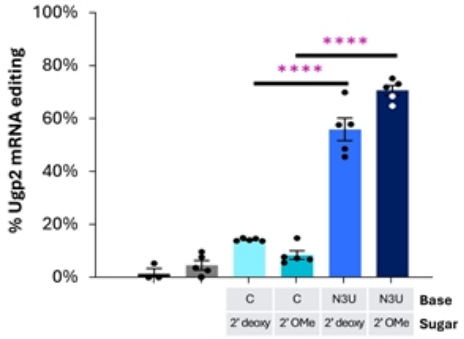
RNAi — SpiNA





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

SpiNA: Stereopure interfering Nucleic Acid
https://wavelifesciences.com/science/publications/

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)

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

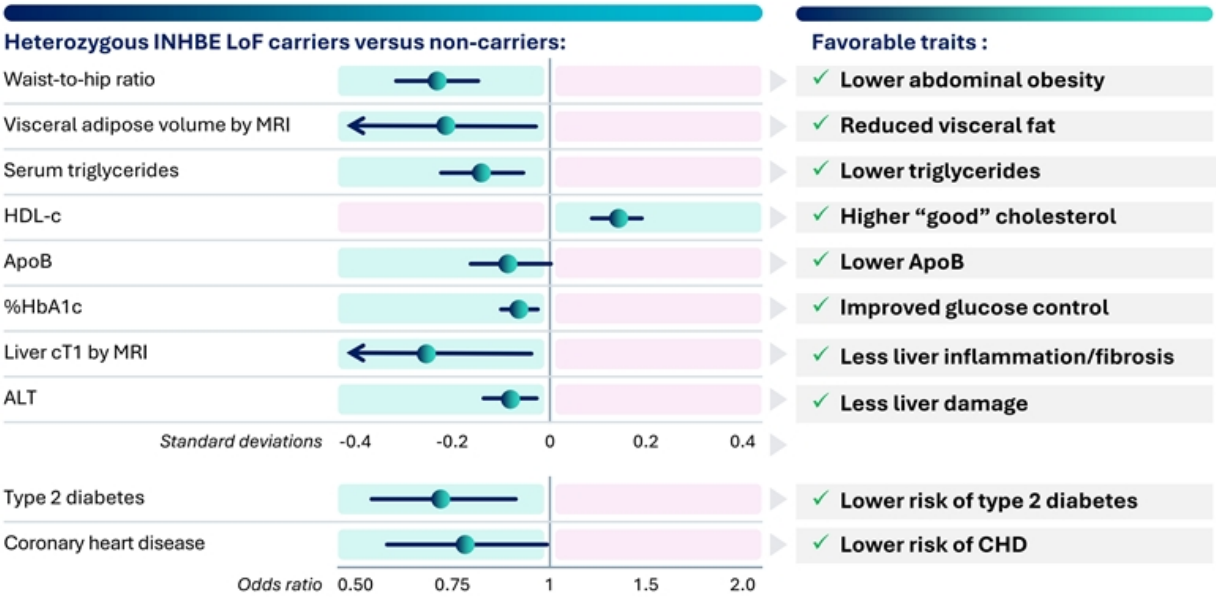
WVE-007

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**

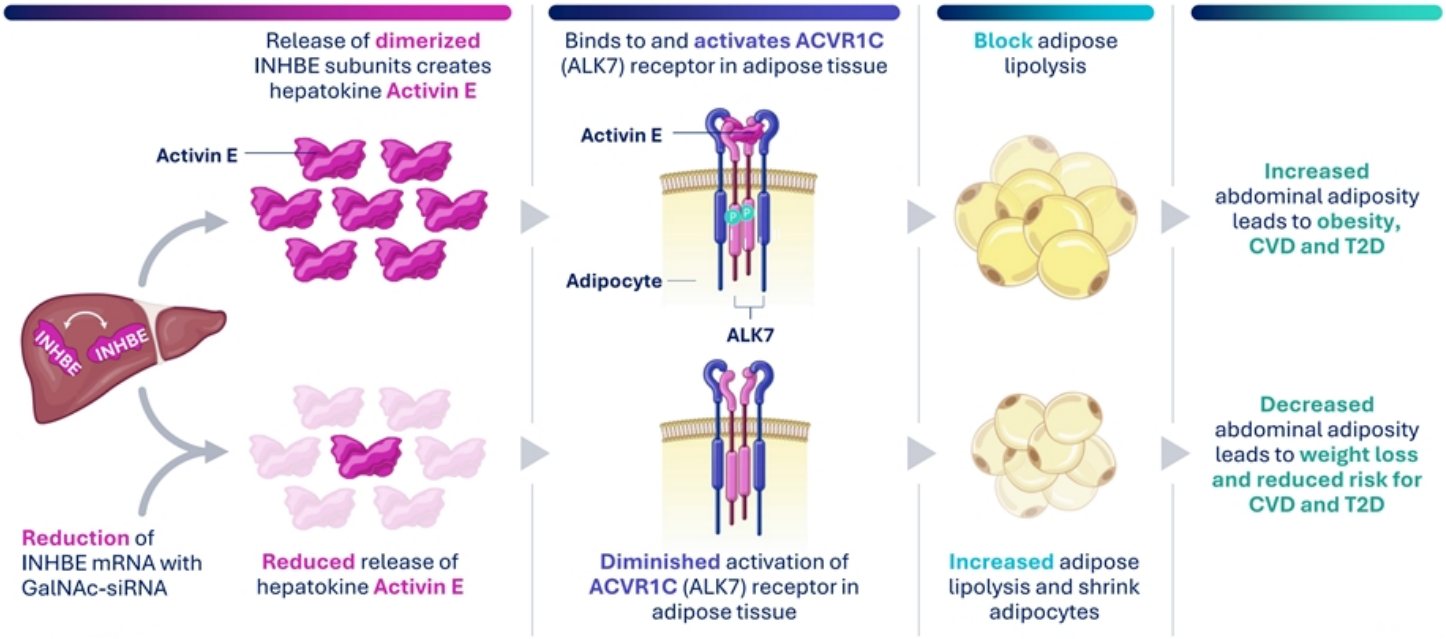
1. Sargeant, et al. 2019 *Endocrinol Metab* (Seoul) 34, 247; 2. Wegovy PI; 3. Ghusn and Hurtado. 2024 *Obesity Pillars* 12, 100127; 4. Leach, et al. 2023 *Prime Therapeutics Claims Analysis*; 5. Gasoyan, et al. 2024 *Obesity* (Silver Spring) 32, 486.

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

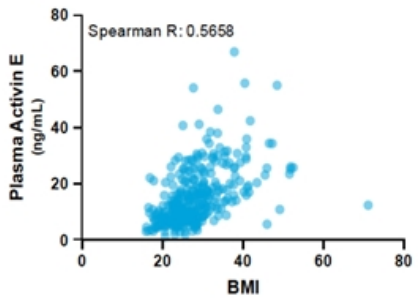
Silencing INHBE mRNA has the potential to treat obesity and associated metabolic diseases



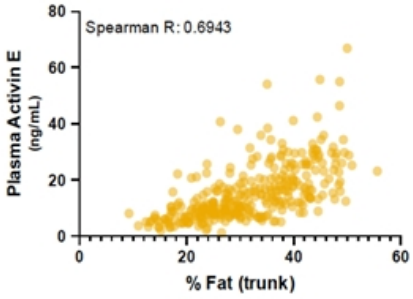
1. Cell Reports (2018) 25, 1193–1203; 2. Biochemical Journal (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8

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

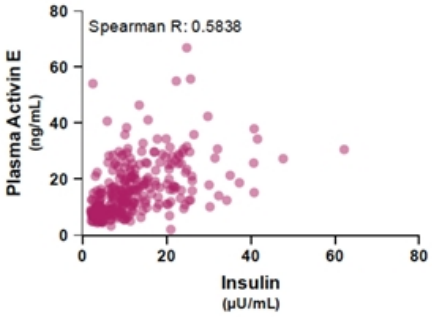
BMI



Abdominal Fat



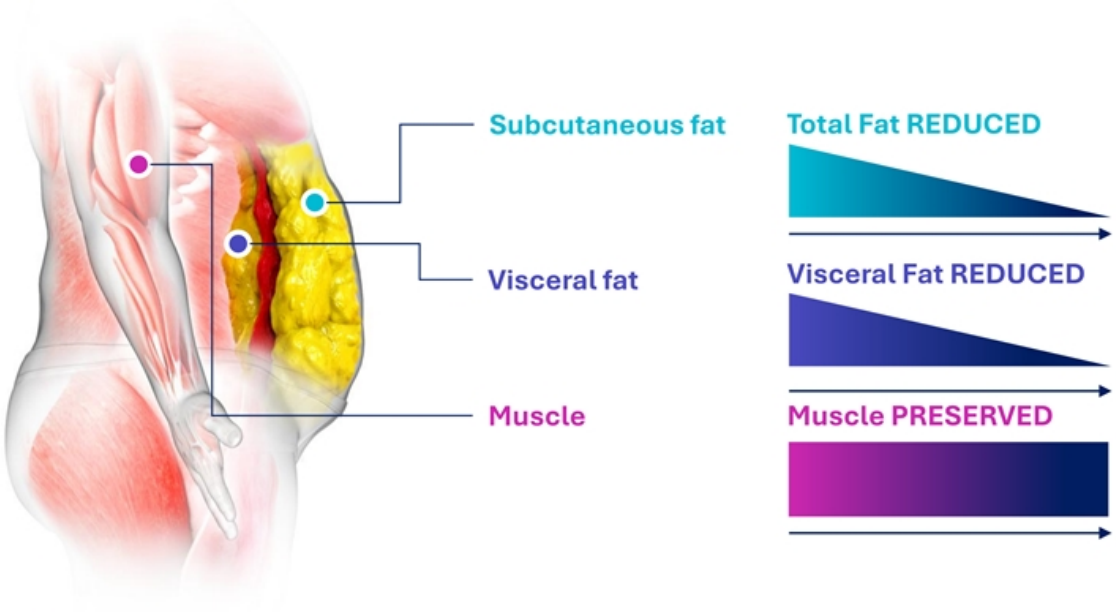
Fasting Insulin



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



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

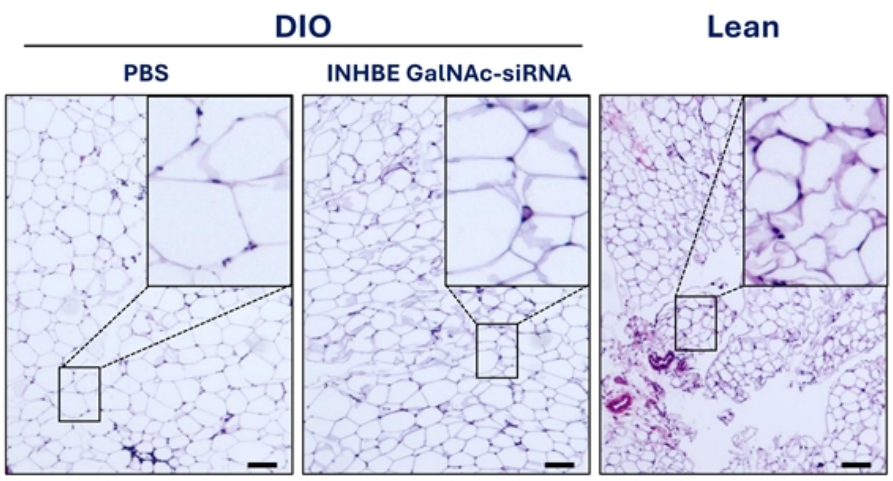


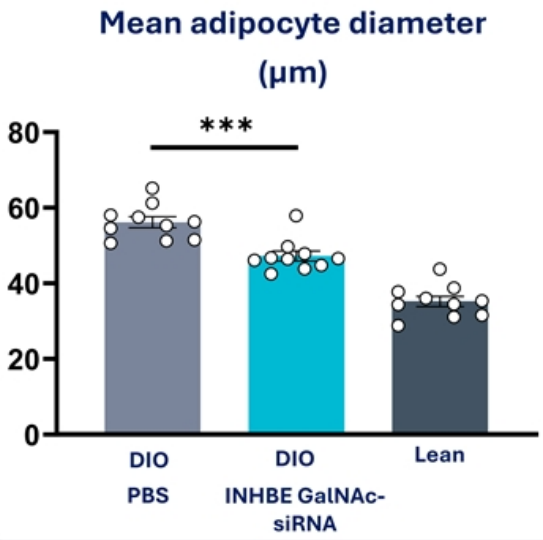
Preservation of muscle mass is linked to many health benefits

- 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.

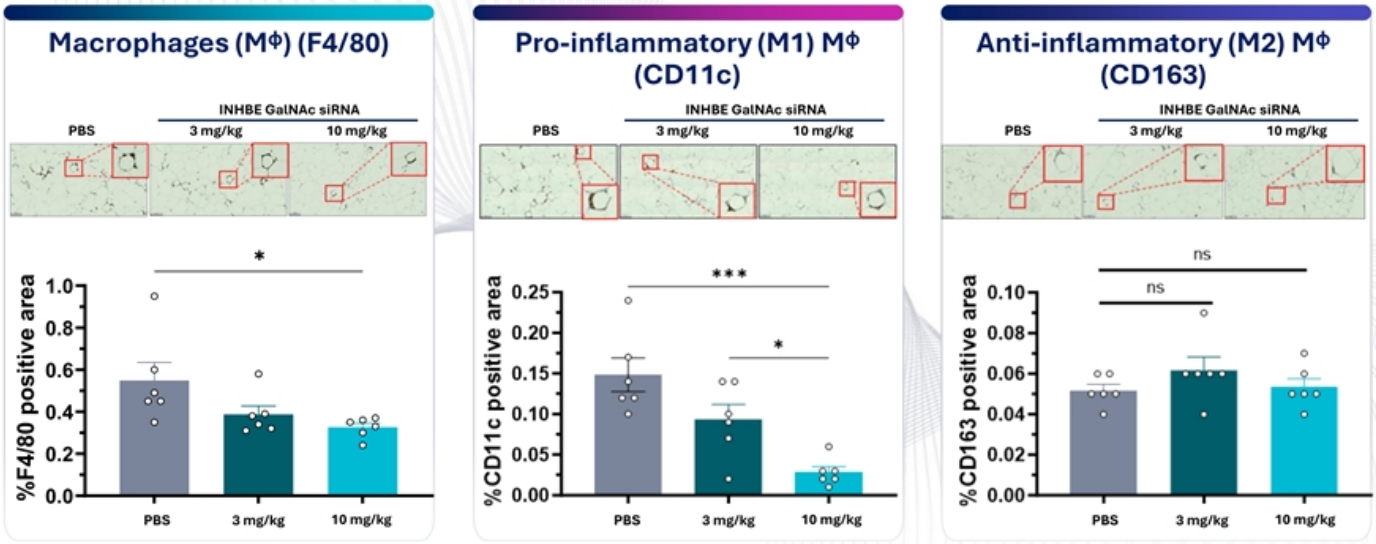
A single dose of INHBE GalNAc-siRNA led to shrinkage of adipocytes in DIO mice





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

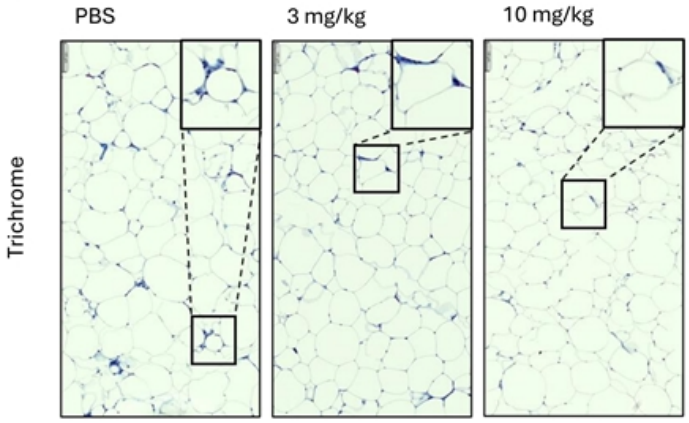
A single dose of INHBE siRNA led to a lower inflammatory state of visceral adipose tissues in DIO mice, with strong suppression of pro-inflammatory M1 macrophages in visceral fat



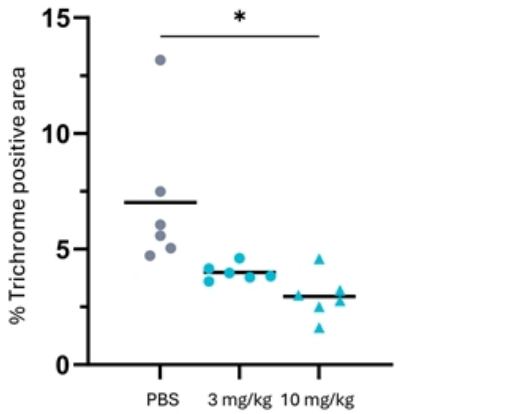
Data presented at ADA Scientific Sessions June 2025
***p<0.001, *p<0.05, ns=non-significant

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

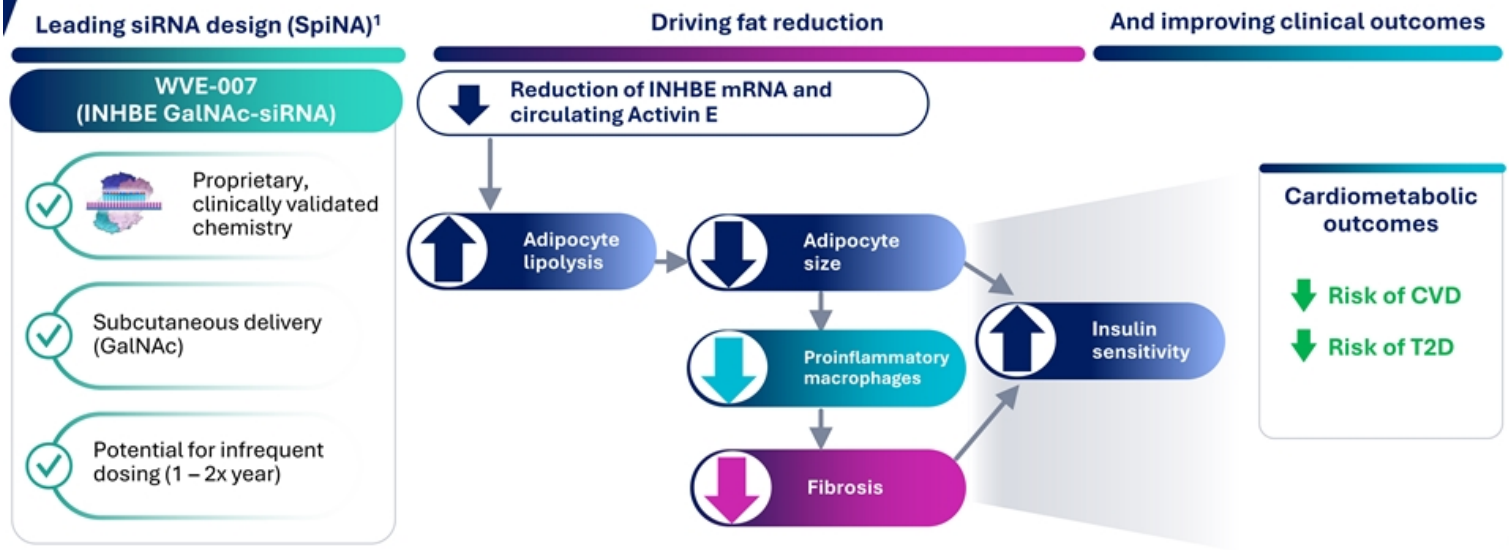


Fibrosis in mouse adipose (Day 56)



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

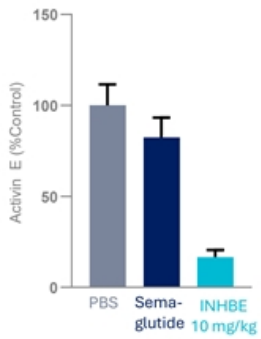


1. SpiNA design is derived from Liu et al., 2023 Nucleic Acids Research doi: 10.1093/nar/gkad268

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

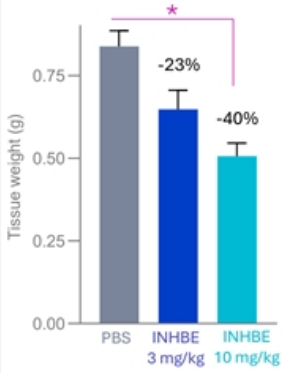
Durable Activin E reduction

Serum Activin E



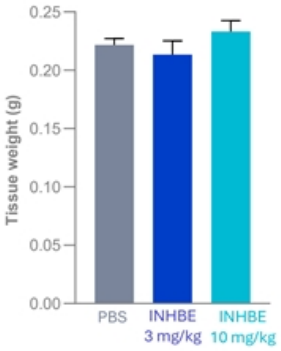
Reduction in fat

Epididymal fat weight



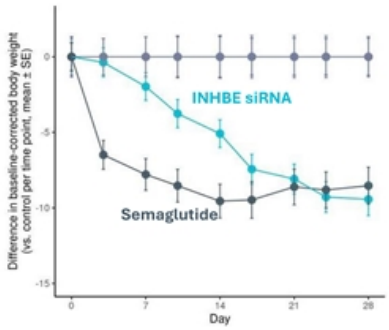
Muscle preservation

Quadricep weight



Reduction in body weight

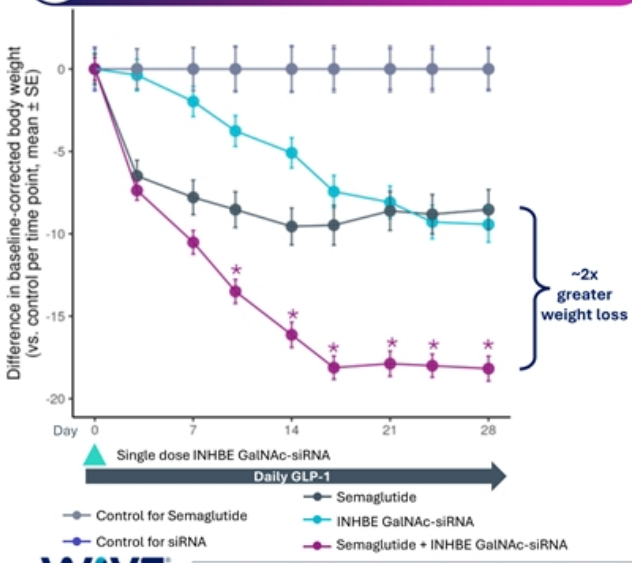
Single dose INHBE GalNAc-siRNA



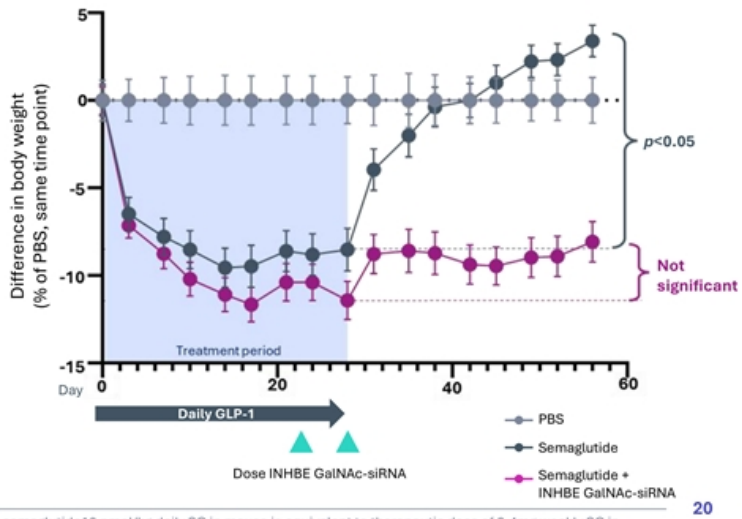
Left and right panels: Semaglutide 10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human; INHBE GalNAc-siRNA 10 mg/kg dose. All data from preclinical studies were conducted in mice fed with 60% high fat diet. Linear Mixed Effects ANOVA with post hoc comparisons of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



WAVE LIFE SCIENCES

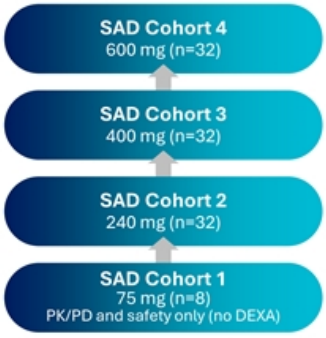
Data from preclinical studies conducted in mice fed with 60% high fat diet; Left: semaglutide10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human. Left Stats: Linear Mixed Effects ANOVA with post hoc comparisons of marginal treatment effects of Semaglutide vs. Semaglutide + 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™

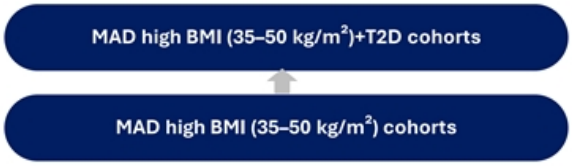
Phase 1 lower BMI (SAD)

- 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



Evaluate safety, tolerability, and PK

Phase 2a high BMI (MAD)



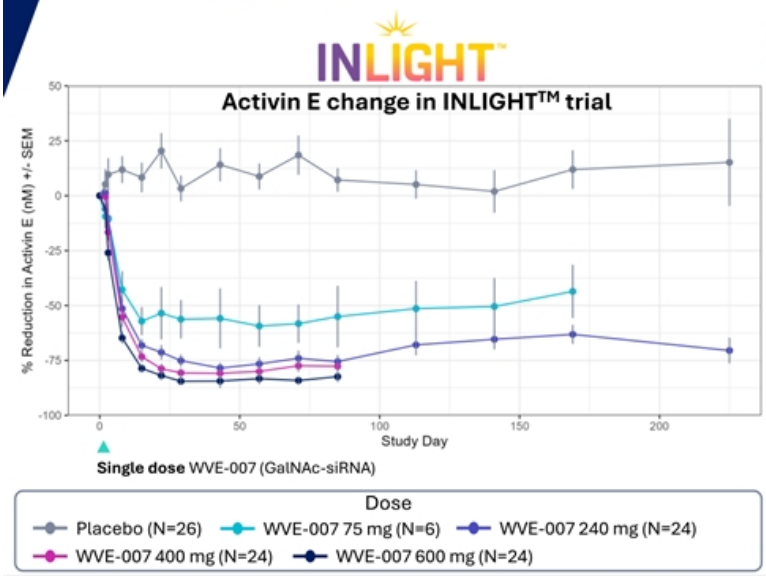
- Individuals with **higher BMI with and without type 2 diabetes**
- Assessments to additionally include:
  - Body composition (MRI in addition to DEXA)
  - Liver fat (MRI-PDFF)
- Diet and exercise modifications included

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

WAVE LIFE SCIENCES

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

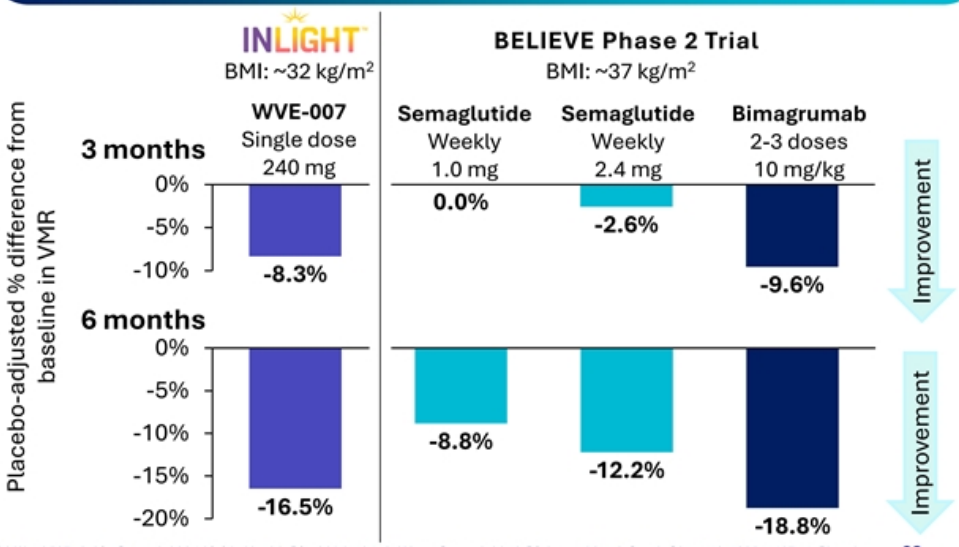
INLIGHT interim Phase 1 data reported March 26, 2026; Left: figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. Right: *p<0.05. All reductions are placebo-adjusted % change from baseline were estimated using an MMRM model with fixed effects for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

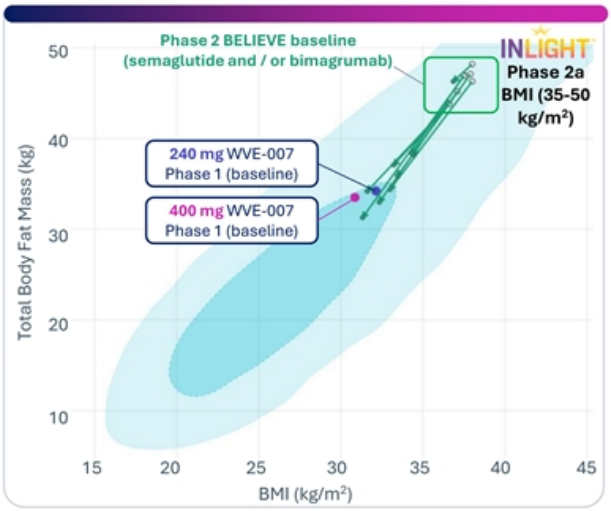


1. Zhang S, *et al.* 2023 *Diabetes Metab Res Rev.* 39(2):e3597; 2. Liu C, *et al.* 2024 *Lipids Health Dis.* 23(1):104; 3. Wang Q, *et al.* 2019 *Diabetes Metab Syndr Obes.* 12:1399-1407. 4. Placebo-corrected VMR calculated based on changes from baseline in visceral fat and lean mass at 3 and 6 mo.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

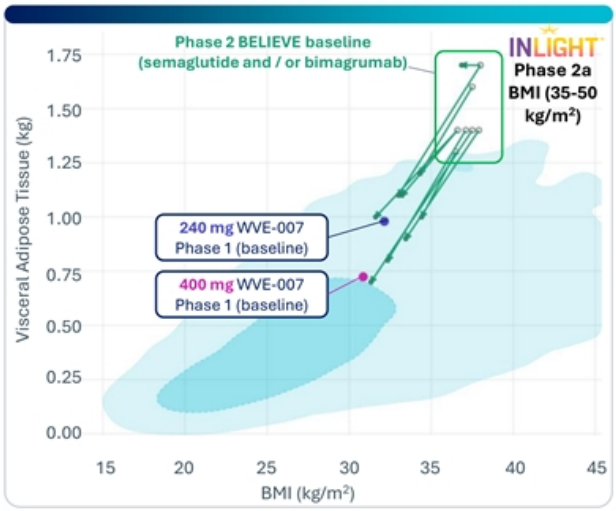
Note: The data presented above are derived from different clinical trials with differences in trial design and patient population, including with respect to BMI. As a result, cross-trial comparisons cannot be made and no head-to-head clinical trials have been conducted.

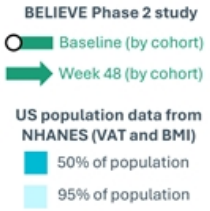
Phase 2a INLIGHT™ trial: higher BMI population aligns with Phase 2 and 3 obesity trials, potential for continued improvements in body composition

Total fat and BMI at baseline



Visceral fat and BMI at baseline



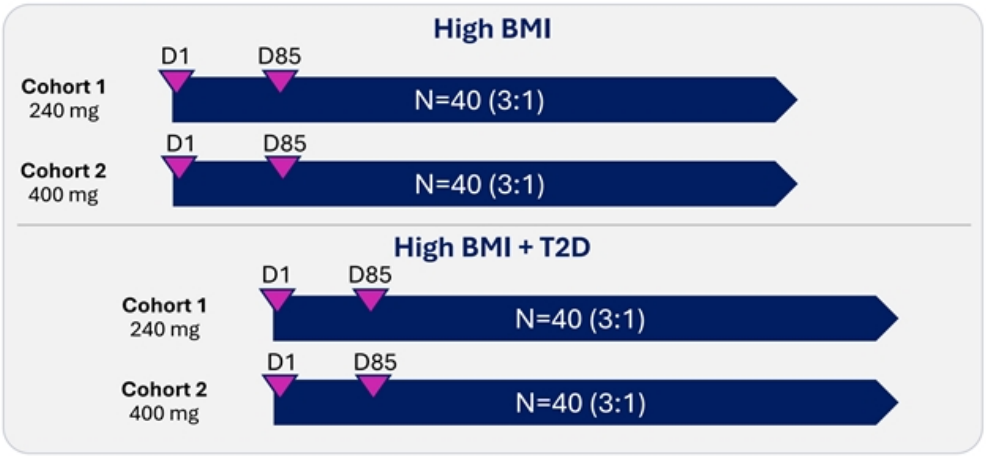


Expect greater fat loss in Phase 2a INLIGHT™ trial in participants with more excess fat

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

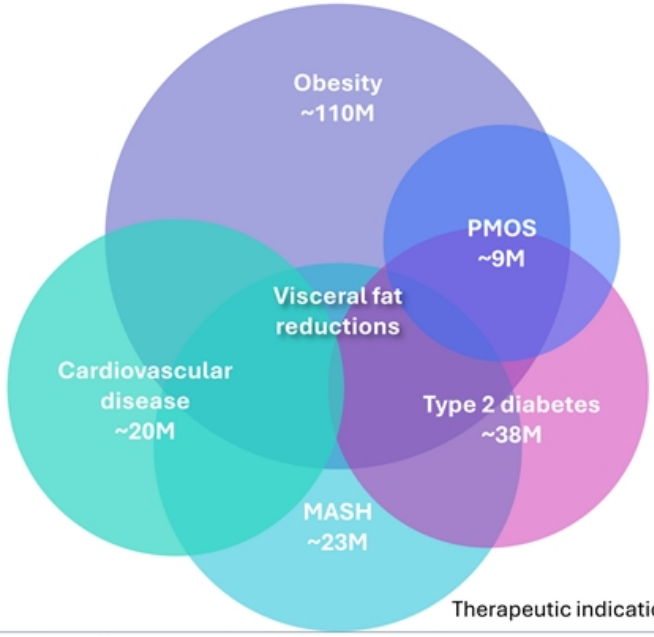
An off-ramp post-incretin treatments

- 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)

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

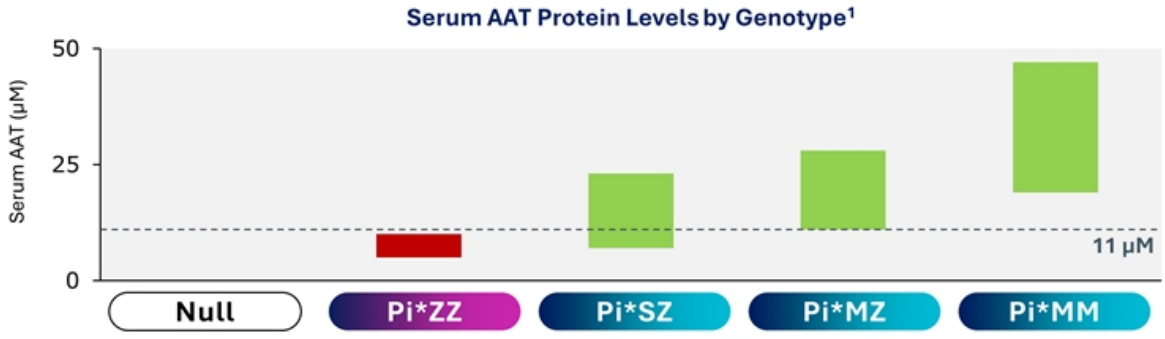
Focused on RNA editing to restore functional AAT, not augmentation

- **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.

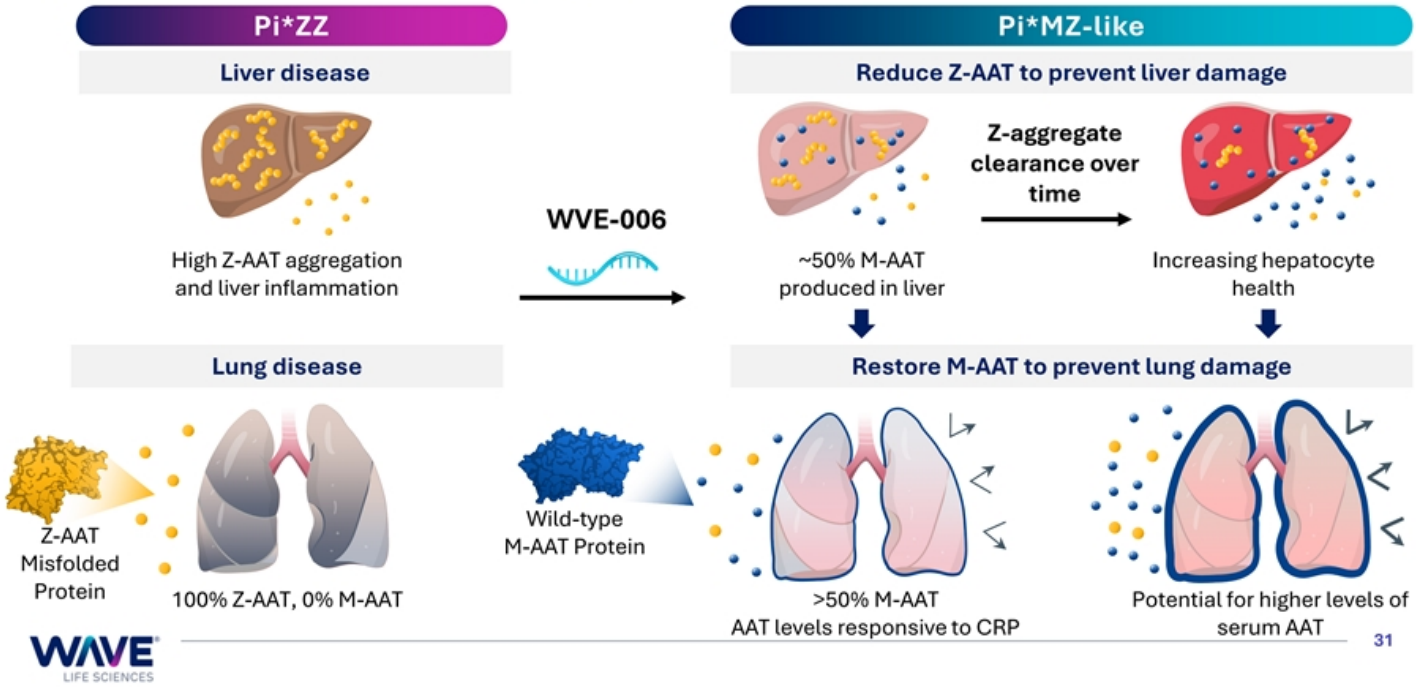
Treatment target: Heterozygous MZ genotype with M-AAT >50% AAT and a dynamic CRP response has low risk of liver and lung disease



	Null	Pi*ZZ	Pi*SZ	Pi*MZ	Pi*MM
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

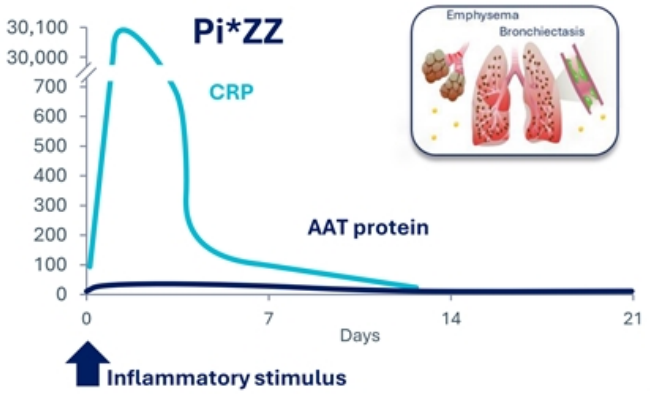
1. Range of observed serum AAT levels from Bornhorst, et al. 2013 CHEST 143:1000-1008; 2. Percent M-AAT of total AAT from a natural history cohort of individuals with M/Z genotype using the same LC-MS/MS assay in RestorAATion-2; 3. Brode, et al. 2012 CMAJ 184:1365-1371; 4. Sanders, et al. 2018 COPD 15:10-16

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

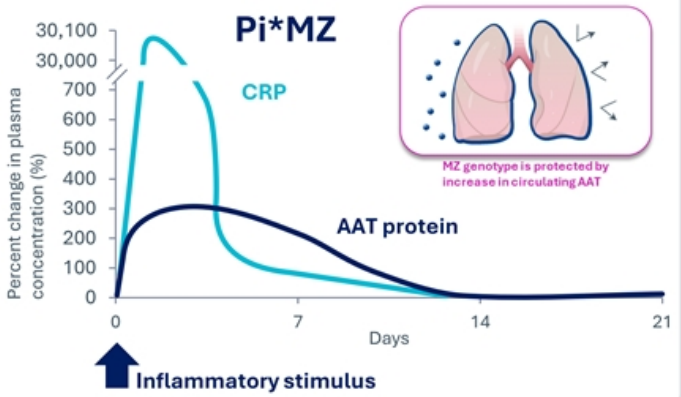


Pi*ZZ individuals have an impaired serum AAT increase during acute-phase responses (APRs), when they need it most

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

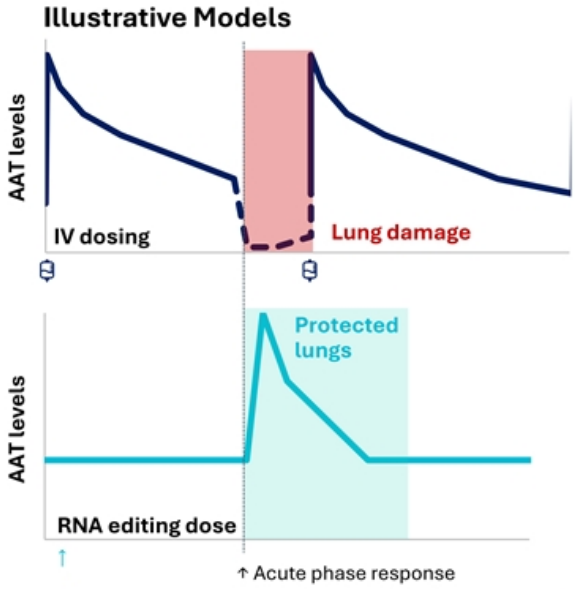
- Even with augmentation therapy, in ZZ individuals, exacerbations occur on average 1–2x yearly
- These exacerbations could deplete AAT levels within hours[1]
- In healthy (including MZ) individuals, AAT levels rise quickly (24–72 hours) after stimulus

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		Safe and convenient
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) CRP increases correlated with AAT increases	• Generally safe and well tolerated • Subcutaneous delivery, with potential for self-administration • Potential for monthly dosing
400 mg monthly	**13.6** µM	**68%** reduction	**59%** M-AAT of total AAT		

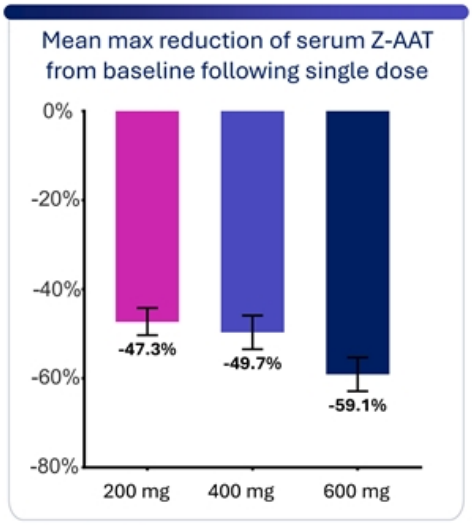
Data from 600 mg monthly dose cohort expected in 2H 2026

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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%).

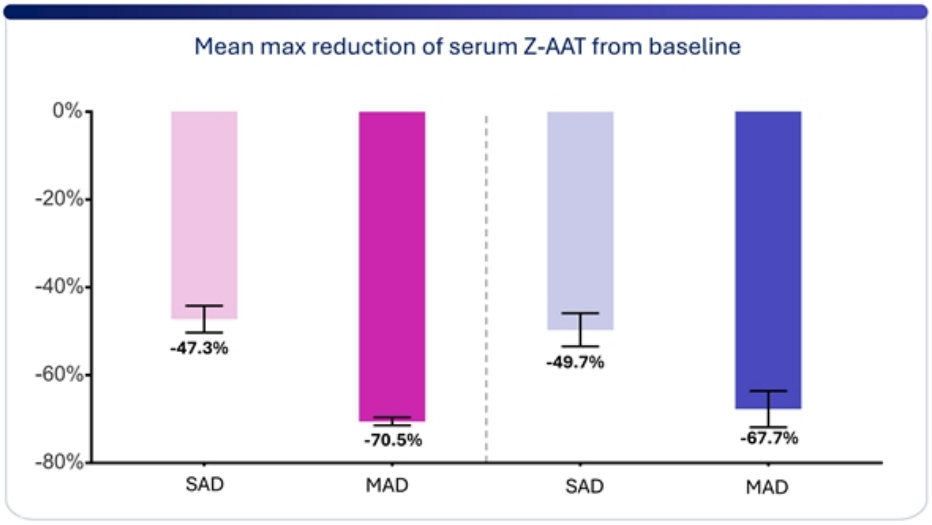
Up to 71% reduction in circulating, mutant Z-AAT supporting potential improvement in liver health

SAD cohorts: Dose-dependent Z-AAT reductions



MAD cohorts: Similar reductions with extended dosing interval

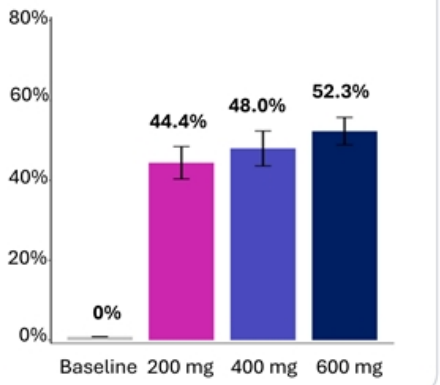
Biweekly (200 mg x 7 doses) | Monthly (400 mg x 4 doses)



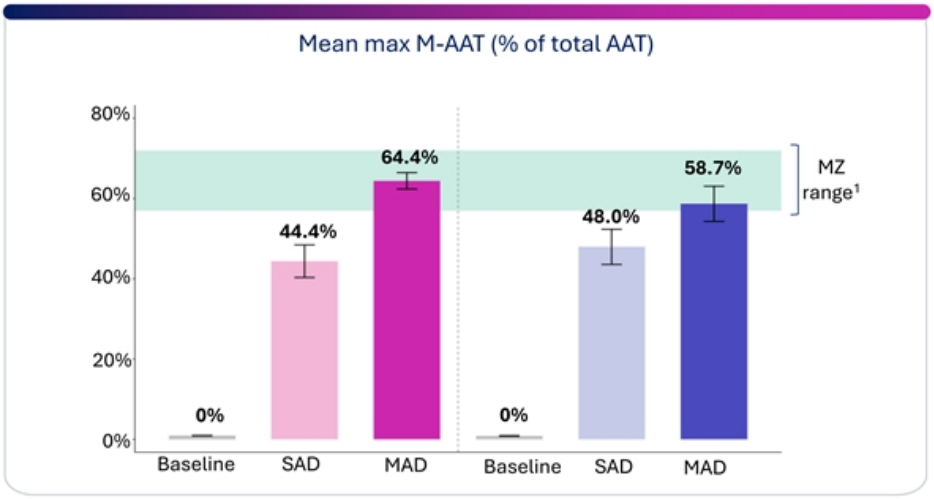
Error bars represent the standard error of the mean (SE).

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



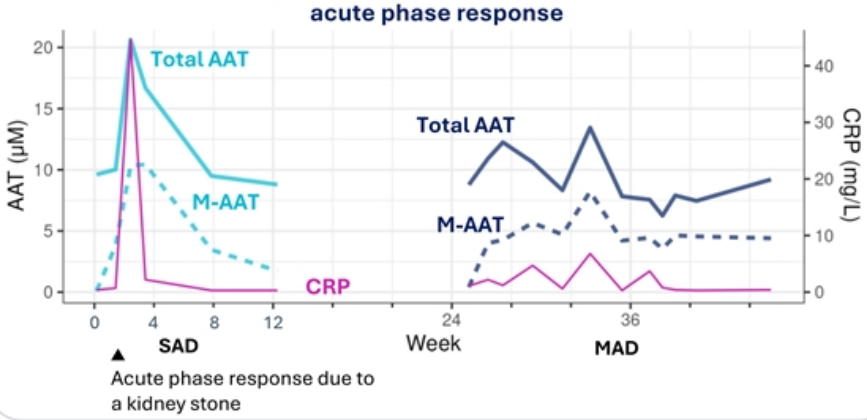
MAD cohorts: Similar M-AAT% with extended dosing interval



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



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]

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



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

WVE-008
RNA editing (AIMer)

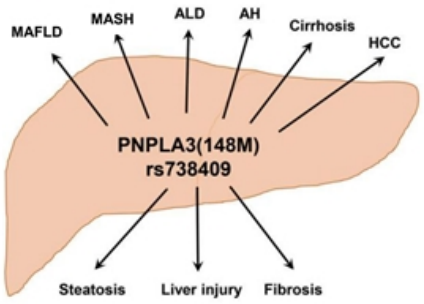
PNPLA3 I148M liver disease

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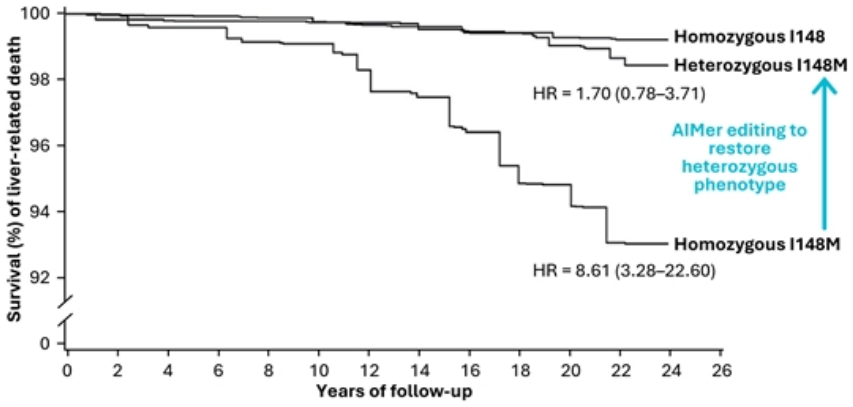
WVE-008 for PNPLA3 I148M liver disease

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



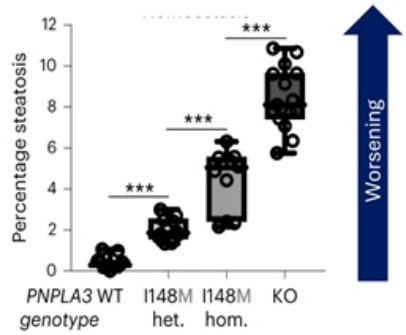
Over nine million homozygous PNPLA3 I148M individuals with genetic liver disease in US and Europe

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

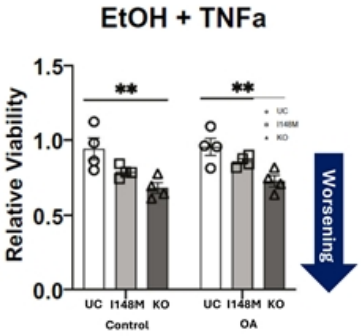
MAFLD, Metabolic dysfunction-associated fatty liver disease; MASH, Metabolic dysfunction-associated steatohepatitis; ALD, alcoholic liver disease; AH, Alcohol-associated hepatitis; HCC, hepatocellular carcinoma

Silencing of PNPLA3 in normal liver may worsen basal physiological functions

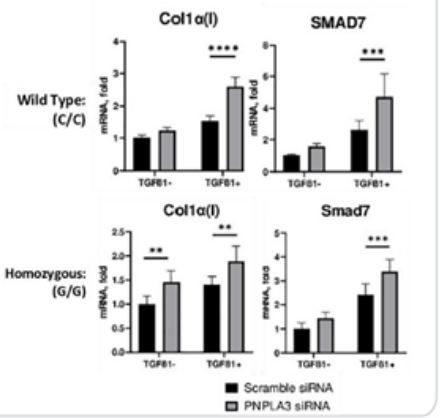
Silencing PNPLA3 worsens steatosis in iPSC-derived human liver organoids[2]



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



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



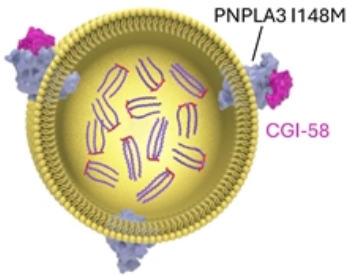
Functional PNPLA3 is imperative for liver health beyond improvements in steatosis

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

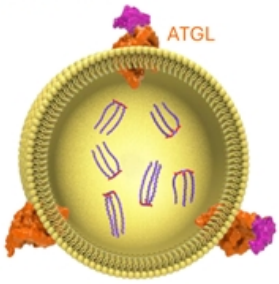
RNA editing approach

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



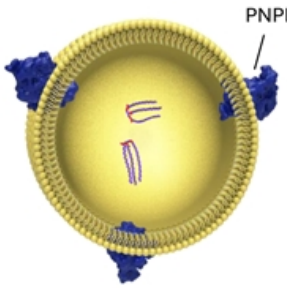
- PNPLA3 I148M accumulates on LDs, sequesters CGI-58, inhibits ATGL's lipase activity and lipid mobilization from ER
- Suppresses retinol metabolism in liver and worsens inflammation and fibrosis
- Promotes liver fat accumulation and fibrosis through activation of stellate cells

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



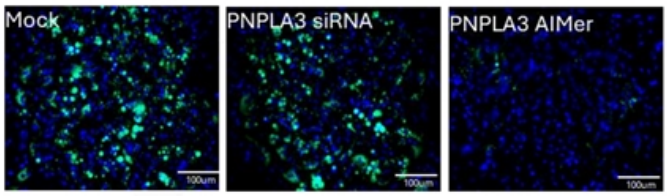
- Restores full PNPLA3 activity
- **Restores lipid mobilization, reverses steatosis, fibrosis, ballooning, and inflammation**

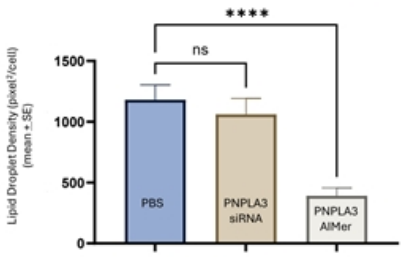
ATGL: adipose triglyceride lipase; CGI-58: co-factor for ATGL; ER endoplasmic reticulum; LDs: lipid droplets; CGI-58 also called ABHD5

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

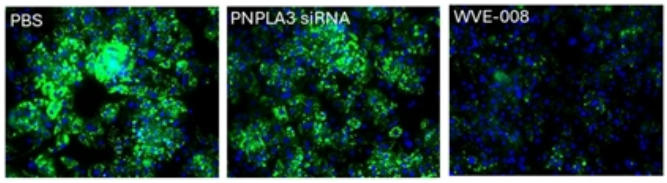
AIMers achieve efficient editing of PNPLA3, leading to reduction of liver fat

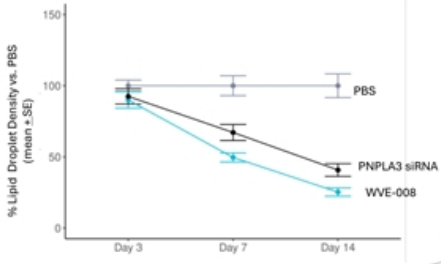
Significant decrease in liver fat with PNPLA3 editing in human HEPATOPAC® model with homozygous I148M





Decrease in liver fat with WVE-008 in monolayer model

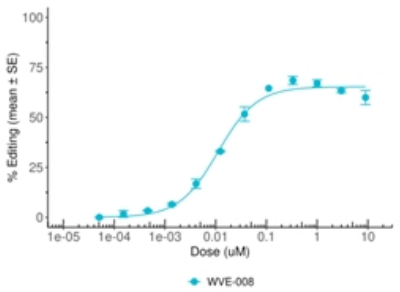




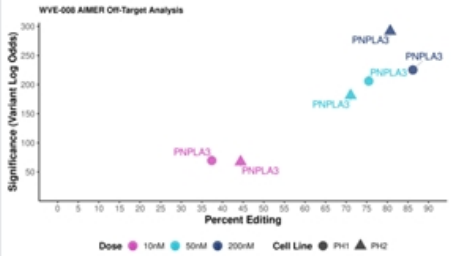
One-way ANOVA with Dunnett post hoc test comparisons to Mock **** P< 0.0001

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

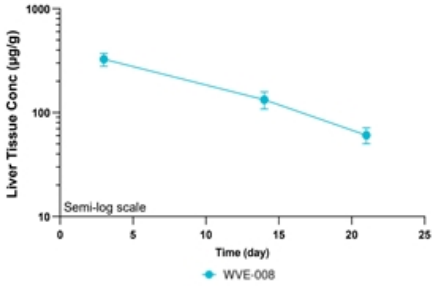
Potential editing with WVE-008



Highly specific editing with WVE-008



Tissue exposure supports excellent delivery



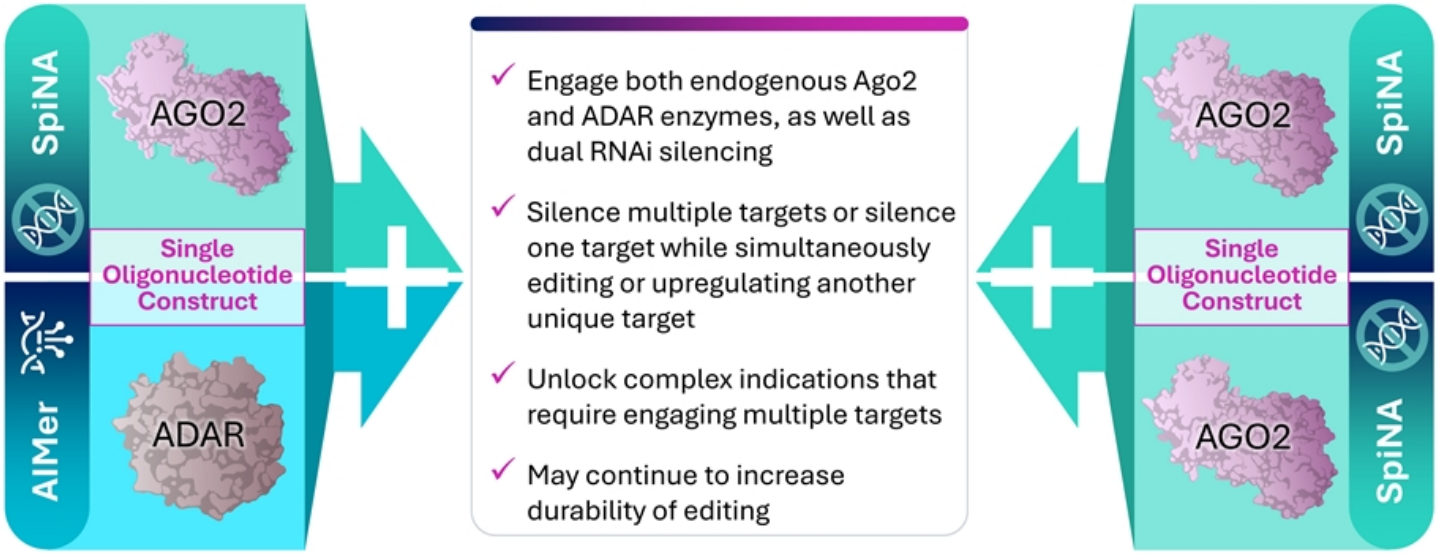
Expect to file Clinical Trial Application (CTA) for WVE-008 in 2H 2026

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

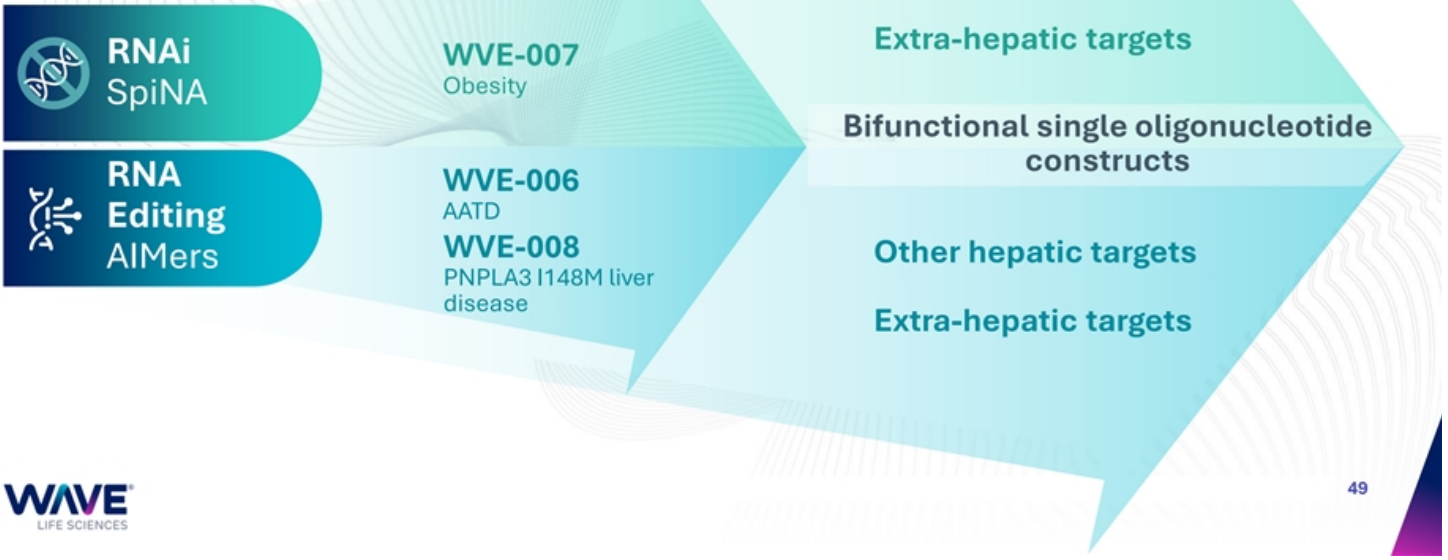
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Reimagining RNA medicines: Bifunctional modalities



- ✓ 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




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For questions contact:
investorrelations@wavelifesci.com