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): January 12, 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:

☐ 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))

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

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. ☐

Item 2.02. Results of Operations and Financial Condition.

On January 12, 2026, Wave Life Sciences Ltd. (the "Company") issued a press release and updated its corporate presentation, as described further under Item 7.01 below, each of which included a preliminary, unaudited estimate of the amount of its cash and cash equivalents as of December 31, 2025. The Company preliminarily estimates that its cash and cash equivalents as of December 31, 2025 were approximately $602 million. A copy of the press release and corporate presentation are furnished as Exhibit 99.1 and Exhibit 99.2 to this Current Report on Form 8-K, respectively.

The information in this Item 2.02 is preliminary, has not been audited and is subject to change pending completion of the Company's audited financial statements for the year ended December 31, 2025. It is possible that the Company or its independent registered public accounting firm may identify items that require the Company to make adjustments to the amount included in this Item 2.02, and such changes could be material. Additional information and disclosures would also be required for a more complete understanding of the Company's financial position and results of operations as of December 31, 2025.

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 January 12, 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 is 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 January 12, 2026.
99.2	Corporate Presentation of Wave Life Sciences Ltd., dated January 12, 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*
Kyle Moran
Chief Financial Officer

Date: January 12, 2026

Wave Life Sciences Highlights Strategic Priorities for 2026 at the 44th Annual J.P. Morgan Healthcare Conference: Accelerating Development of WVE-007 (INHBE siRNA) for Obesity and Rapidly Advancing RNA Editing Portfolio

Wave expects to initiate a Phase 2a multidose portion of WVE-007 INLIGHT clinical trial in individuals living with obesity with higher BMI and comorbidities in 1H 2026, and initiate new trials of WVE-007 as an add-on to incretin and as post-incretin maintenance in 2026

Initial WVE-007 240 mg single-dose data reported in 2025 demonstrated improved body composition with fat loss similar to GLP-1 at three months with muscle preservation and the potential for once or twice-yearly dosing; higher dose and longer follow-up data from INLIGHT anticipated in 2026, including three-month 400 mg and six-month 240 mg data on track for this quarter

Extending leadership in RNA editing following first-ever successful clinical translation with WVE-006 for AATD, with multiple additional data updates from RestorAATion-2 on track for 2026; Wave expects to file CTA in 2026 for WVE-008 for nine million individuals living with homozygous PNPLA3 I148M liver disease in the U.S. and Europe

Well capitalized with preliminary, unaudited cash and cash equivalents of ~$602 million as of December 31, 2025; expected cash runway into 3Q 2028

Presentation and webcast at 44th Annual J.P. Morgan Healthcare Conference tomorrow, Tuesday, January 13, 2026 at 2:15 p.m. PT / 5:15 p.m. ET

CAMBRIDGE, Mass., January 12, 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 highlighted its strategic priorities for 2026, including accelerating development of WVE-007, an investigational INHBE GalNAc-siRNA for obesity, and rapidly advancing its RNA editing portfolio, ahead of the company's scheduled presentation at the 44th Annual J.P. Morgan Healthcare Conference.

"At Wave, we are using our novel chemistry to translate powerful human genetic insights into potentially transformational RNA medicines. As we enter 2026, we are seeing the continued translation of our portfolio in the clinic, as most recently evidenced by our December data for WVE-007, our INHBE-siRNA for obesity. After only three months, at the lowest single therapeutic dose of WVE-007, we are seeing a differentiated profile with fat loss on par with semaglutide, favorable safety and tolerability, as well as the potential for once or twice a year dosing. With multiple near-term catalysts ahead and an accelerated development plan, we believe we are well positioned and well capitalized to deliver a potentially transformational treatment for obesity," said Paul Bolno, MD, MBA, President and Chief Executive Officer at Wave Life Sciences. "And in RNA editing, we have made history in the field with the first ever clinical translation of RNA editing with WVE-006 for AATD, and we are building on this success with WVE-008, which aims to address the nine million individuals living with homozygous PNPLA3 I148M liver disease in the U.S. and Europe. We continue to push the boundaries of what is possible with oligonucleotides. Further, the ability to combine our best-in-class, clinically-validated RNA editing and RNAi capabilities into a single bifunctional construct has the potential to expand our addressable therapeutic areas further and let us reach even more patients."

Recent clinical data updates and anticipated 2026 milestones

RNAi – WVE-007 for obesity

- WVE-007 is an investigational INHBE GalNAc-siRNA using Wave's proprietary SpiNA design. Silencing INHBE mRNA is a promising therapeutic strategy to treat obesity with strong evidence from human genetics.
- In preclinical studies, a single dose of Wave's INHBE GalNAc-siRNA led to weight loss similar to GLP-1 (semaglutide), which was driven by substantial decreases in fat mass and preservation of lean mass in DIO mice. As an add-on to semaglutide, Wave observed double the weight loss in mice compared to semaglutide alone, and in a separate study it prevented weight regain upon cessation of semaglutide.
- In the INLIGHT clinical trial, a single 240 mg dose of WVE-007 demonstrated improved body composition with fat loss similar to GLP-1 at three months with muscle preservation in healthy individuals with overweight or obesity and an average BMI of 32.1 kg/m². INLIGHT does not include any diet or exercise modifications. There was sustained and robust suppression of serum Activin E supporting once-or twice-yearly dosing. WVE-007 was generally safe and well tolerated.
- The 240 mg (n=32), 400 mg (n=32), and 600 mg (n=32) single dose cohorts of INLIGHT are fully dosed. In the first quarter of 2026, Wave expects to deliver six-month follow-up data from the 240 mg single-dose cohort, as well as three-month follow-up data from the 400 mg single dose cohort. In the second quarter of 2026, Wave expects to deliver six-month follow-up data from the 400 mg single dose cohort and three-month follow-up data from the 600 mg single dose cohort.
- Wave expects to initiate a Phase 2a multidose portion of the ongoing INLIGHT clinical trial in individuals living with obesity with higher BMI and comorbidities in the first half of 2026.
- Wave also expects to initiate new clinical trials evaluating WVE-007 as an add-on to incretin and as post-incretin maintenance in 2026.

RNA editing

WVE-006 (AATD)

- WVE-006 is an investigational GalNAc-conjugated RNA editing oligonucleotide (AIMer) that is uniquely designed to address alpha-1 antitrypsin deficiency (AATD)-related lung disease, liver disease, or both. In September 2025, Wave announced clinical data from the 200 mg single and multidose cohorts and the 400 mg single dose cohort of RestorAATion-2. WVE-006 achieved key AATD treatment goals, recapitulating the MZ phenotype, including the ability to dynamically generate AAT protein during an acute phase response.
- The RestorAATion-2 clinical trial is ongoing and data from the 400 mg multidose cohort are expected in the first quarter of 2026. Single and multidose data from the 600 mg cohort (the third and final cohort in the trial) are expected in 2026.

WVE-008 (liver disease)

- Wave is building on clinical success in RNA editing by advancing WVE-008, a GalNAc-conjugated AIMer for homozygous PNPLA3 I148M liver disease. There are an estimated nine million individuals living with homozygous PNPLA3 I148M liver disease in the U.S. and Europe. The PNPLA3 I148M variant is a well-established driver of steatosis, inflammation, ballooning, and fibrosis; however, there are no approved medicines that directly address this biology. In preclinical studies, Wave has demonstrated that RNA editing results in restoration of functional PNPLA3 protein and superior reduction of liver fat as compared to silencing approaches.
- Wave is on track to file a Clinical Trial Application (CTA) for WVE-008 in 2026.

New bifunctional modality (RNAi and RNA editing)

- Wave is applying its chemistry to innovate a new bifunctional modality with a single oligonucleotide construct designed to silence one target while simultaneously editing or upregulating another distinct target. During its 2025 Research Day, Wave presented preclinical data demonstrating simultaneous upregulation of LDLR and silencing of PCSK9 in a preclinical study. Wave expects to provide further updates on its bifunctional modality in 2026.

Additional clinical programs

- WVE-N531 is an investigational exon skipping oligonucleotide being developed as a disease modifying treatment for boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. Wave remains on track to file a New Drug Application (NDA) in 2026 to support accelerated approval of WVE-N531 with monthly dosing.
- WVE-003 is a first-in-class, allele-selective investigational oligonucleotide for the treatment of Huntington's disease (HD). Wave has prepared an Investigational New Drug (IND) application for a potentially registrational Phase 2/3 study of WVE-003 and would plan to submit it in conjunction with a prospective strategic partner.

Preliminary year-end cash position

Wave is well capitalized with preliminary, unaudited cash and cash equivalents of ~$602 million as of December 31, 2025, with expected cash runway into 3Q 2028. These preliminary, unaudited results are subject to adjustment. Wave expects to report its final and complete fourth-quarter and full-year 2025 financial results in late February 2026, and the actual results could be different from these preliminary, unaudited financial results.

Upcoming presentation at J.P. Morgan Healthcare Conference

Paul Bolno, MD, MBA, President and Chief Executive Officer, is scheduled to present at the 44th Annual J.P. Morgan Healthcare Conference in San Francisco, CA on Tuesday, January 13, 2026 at 2:15 p.m. PT / 5:15 p.m. ET. A live webcast of the presentation can be accessed by visiting "Investor Events" on the Investors section of the Wave Life Sciences website: https://ir.wavelifesciences.com/events-publications/events. A replay of this presentation will be archived and available on the site for a limited time following the event.

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 RNA medicines platform, PRISM®, 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 includes RNAi, editing, splicing, and antisense silencing, providing Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's diversified pipeline includes clinical programs in obesity, alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy, and Huntington's disease, as well as several preclinical programs utilizing the company's broad RNA therapeutics toolkit. 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 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, dosing regimen, safety profile, 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 anticipated status and progress of our programs relative to potential competitors and how our programs differ from competitors' programs; the potential commercialization of our programs the patient population estimates 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 RNAi and RNA editing capabilities, including our AIMers; our potential to innovate a new bifunctional modality and the anticipated therapeutics benefits of such modality; the potential benefits of our Stereopure interfering Nucleic Acid (SpiNA) next generation siRNA design; 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 preliminary, unaudited cash and cash equivalents as of December 31, 2025; the anticipated timing of any announcements related to our financial results; 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 enter into new and/or maintain existing strategic partnerships; 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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Exhibit 99.2

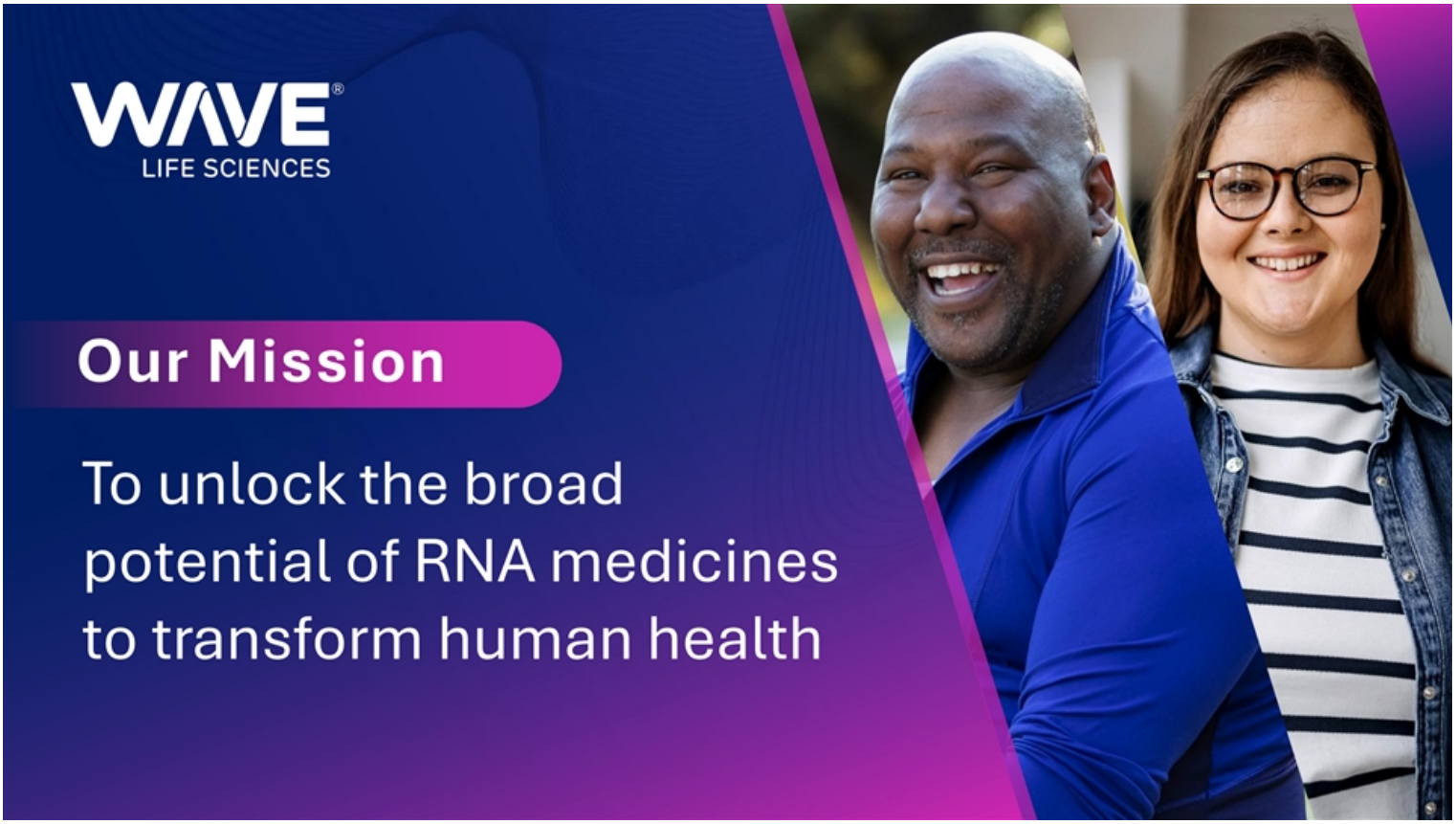
Wave Life Sciences

Corporate Presentation

January 12, 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

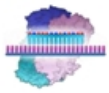
Differentiated RNA medicines platform and chemistry

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

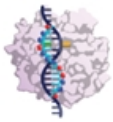
RNAi



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: **DMD** and **HD** clinical programs

Unlocking emerging pipeline

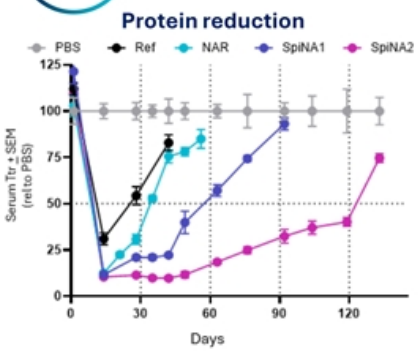
- **Extra-hepatic capabilities:** with RNAi and RNA editing
- **Novel bifunctional modality:** simultaneously edit and silence with single oligonucleotide construct

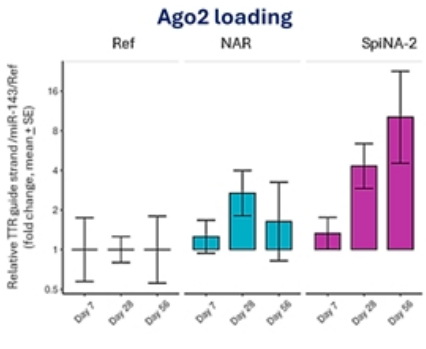
Well capitalized with ~$602 million[1] and expected cash runway into 3Q 2028

[1] Preliminary, unaudited cash and cash equivalents of ~$602 million are as of December 31, 2025. These preliminary, unaudited results are subject to adjustment. Wave expects to report its final and complete fourth-quarter and full-year 2025 financial results in late February 2026, and the actual results could be different from these preliminary, unaudited financial results

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

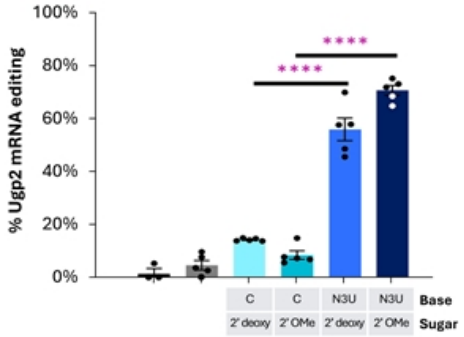
RNAi — SpiNA





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, diversified RNA medicines pipeline including first-in-class RNA editing and RNAi programs

Program	Discovery	IND / CTA Enabling Studies	Clinical	Rights	Patient population (US & Europe)
RNAi					
WVE-007 (GalNAc) INHBE (obesity)				100% global	175M (>1 billion globally)
GalNAc / extra-hepatic Multiple				100% global	--
RNA EDITING					
WVE-006 (GalNAc) SERPINA1 (AATD)				GSK exclusive global license	200K
WVE-008 (GalNAc) PNPLA3 (liver disease)				100% global	9M
GalNAc / extra-hepatic Multiple				100% global	--
SPLICING					
WVE-N531 Exon 53 (DMD)				100% global	2.3K
Other exons (DMD)				100% global	Up to 18K
ALLELE-SELECTIVE SILENCING					
WVE-003 mHTT (HD)				100% global	25K Symptomatic (SNP3) 60K Pre-Symptomatic (SNP3)

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

WVE-007
GalNAc-siRNA silencing

Obesity

WAVE LIFE SCIENCES

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

Individuals living with **obesity** have higher risk for many serious health conditions, including heart disease, type 2 diabetes, and some forms of cancer[1]

Current standard of care: GLP-1s

Impact of GLP-1s is often limited by:

- Loss of muscle mass[2]
- Frequent dosing[3]
- Poor tolerability[4]
- High discontinuation rates[5,6]

WVE-007

(INHBE GalNAc-siRNA)

- **Fat loss similar to GLP-1 at three months**
- **Preserves muscle**
- **Potential 1–2 per year dosing**
- **Generally safe and well-tolerated**

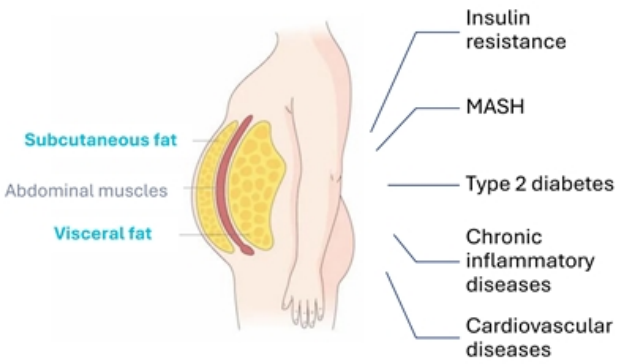
Improving body composition is the future for the > 1 billion people living with obesity globally

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

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

Reduce fat, including visceral fat

Increased visceral adiposity is associated with many diseases including cardiometabolic disorders

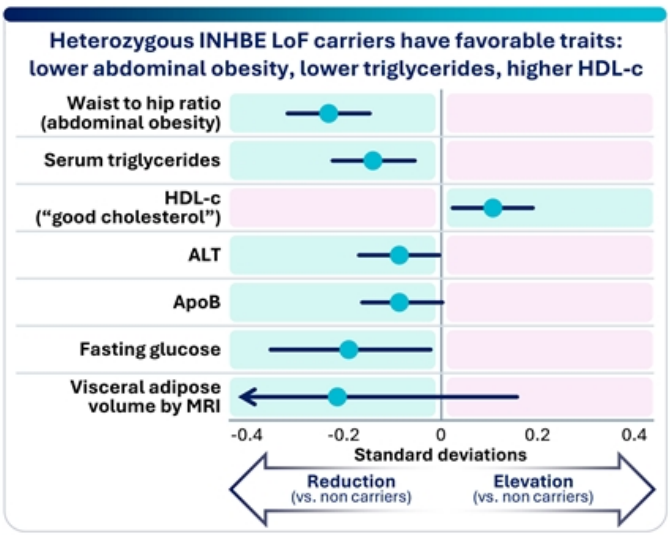


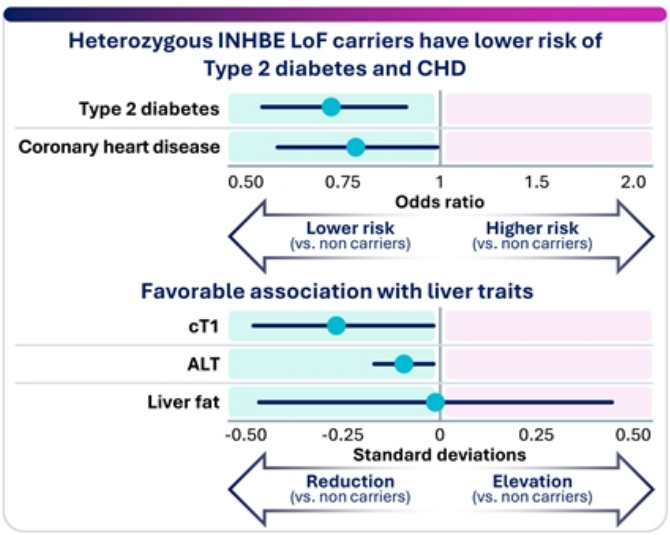
Preserve lean mass, including muscle

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

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

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



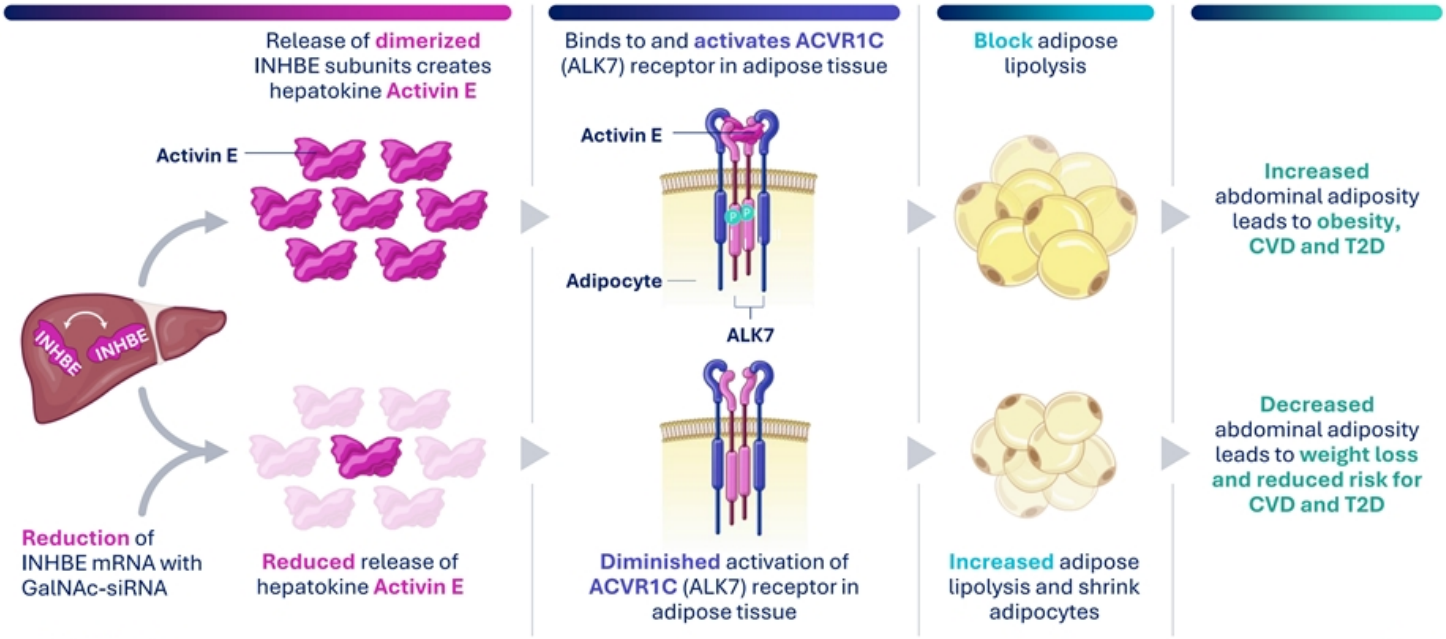


Silencing INHBE mRNA by ≥50% is expected to recapitulate the healthy metabolic profile of heterozygous INHBE LoF carriers

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

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

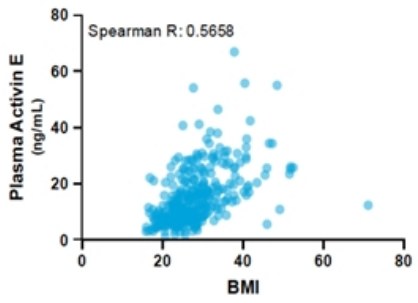
Silencing INHBE mRNA has potential to treat obesity and associated metabolic diseases



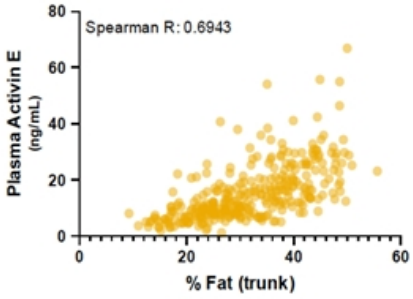
1. Cell Reports (2018) 25, 1193–1203; 2. Biochemical Journal (2024) 481 547–564; 3. PNAS 2023 Vol. 120 No. 32 e2309967120; 4. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 5. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8

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

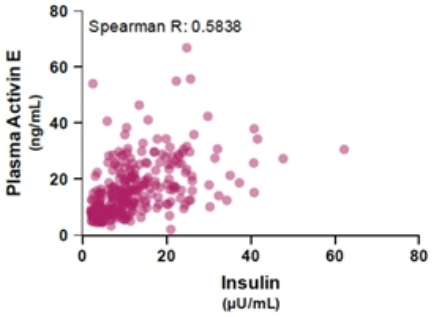
BMI



Abdominal Fat



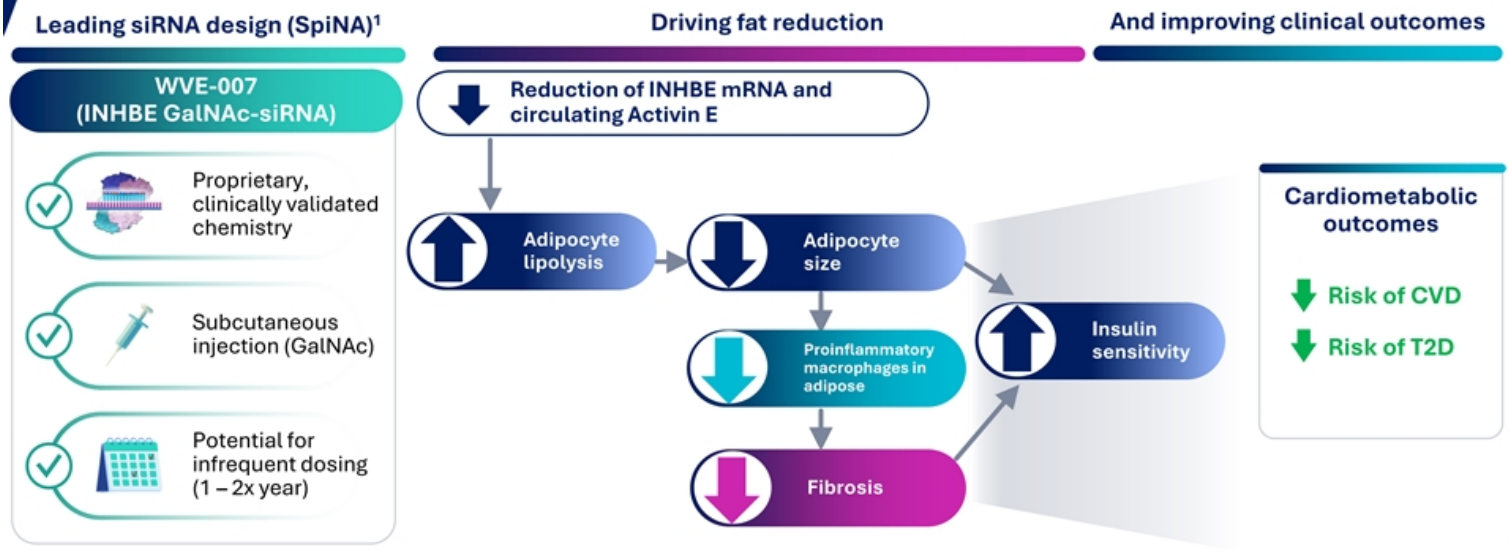
Fasting Insulin



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

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

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

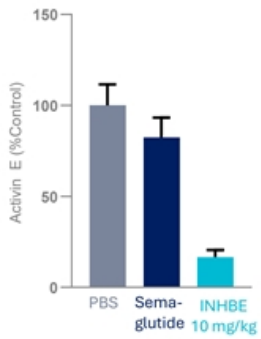


1. SpiNA design is derived from Liu et al., 2023 Nucleic Acids Research doi: 10.1093/nar/gkad268

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

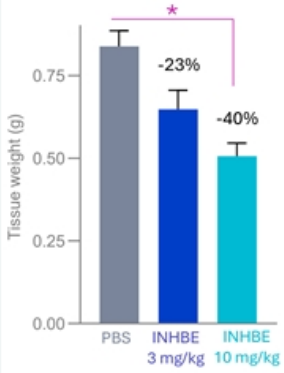
Durable Activin E reduction

Serum Activin E



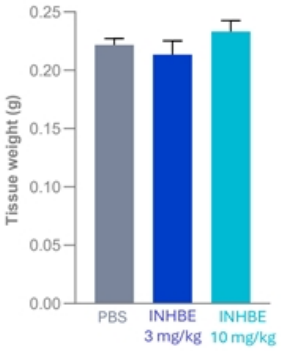
Reduction in fat

Epididymal fat weight



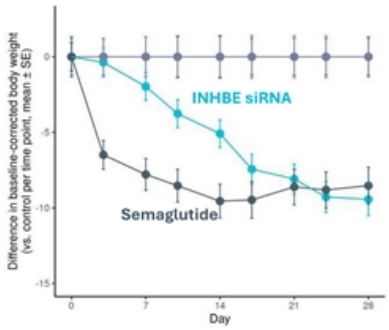
Muscle preservation

Quadricep weight



Reduction in body weight

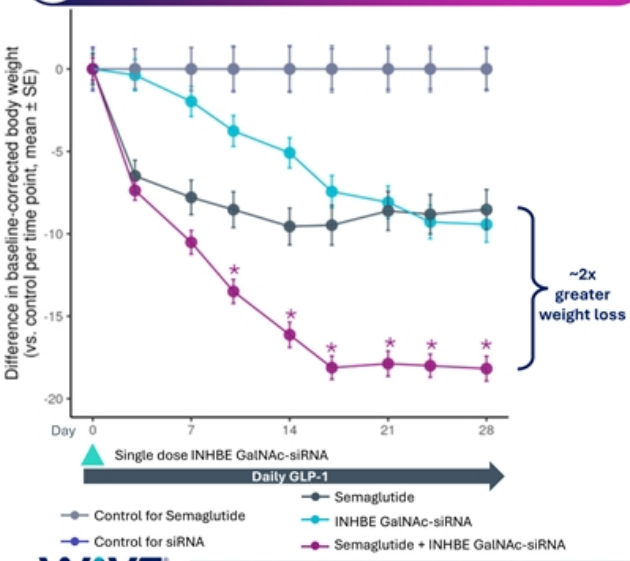
Single dose INHBE GalNAc-siRNA



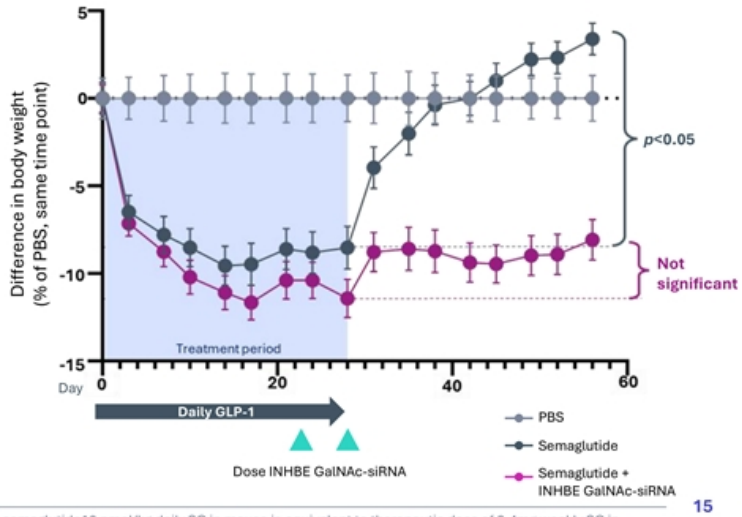
Left and right panels: Semaglutide 10 nmol/kg daily SC in mouse is equivalent to therapeutic dose of 2.4mg weekly SC in human; INHBE GalNAc-siRNA 10 mg/kg dose. All data from preclinical studies were conducted in mice fed with 60% high fat diet. Linear Mixed Effects ANOVA with post hoc comparisons of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

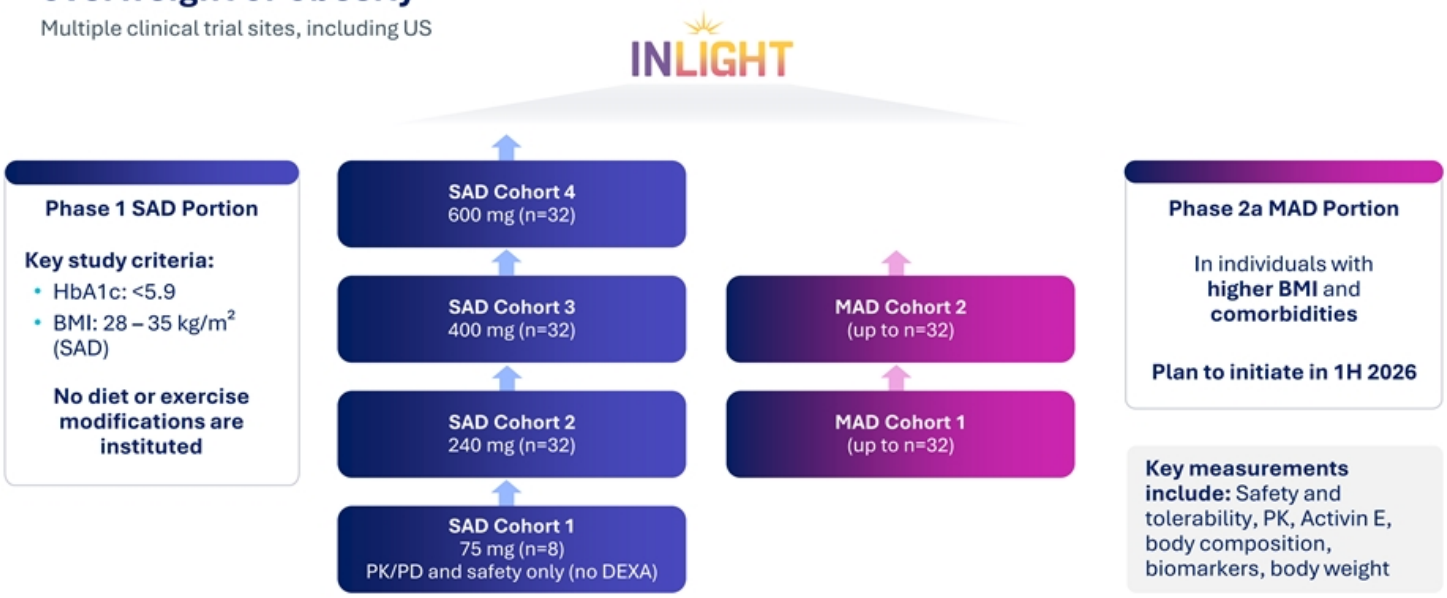


WAVE LIFE SCIENCES

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

INLIGHT: Clinical trial of WVE-007 in otherwise healthy individuals living with overweight or obesity

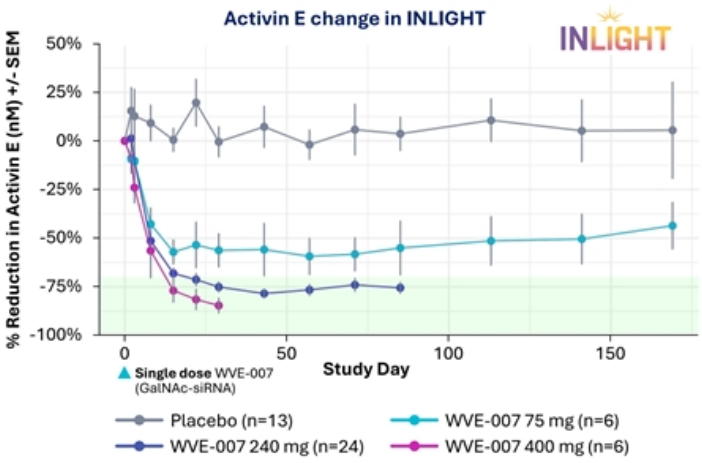
Multiple clinical trial sites, including US



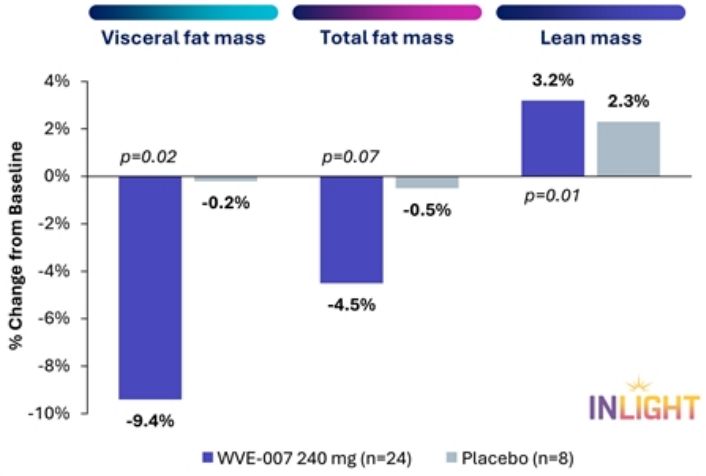
SAD: single-ascending dose; MAD: multi-ascending dose; PK: pharmacokinetics; PD: pharmacodynamics
Randomized, double-blind, placebo-controlled (3:1) study of ascending doses of WVE-007

Improvements in body composition observed at three months after a single WVE-007 dose (lowest therapeutic dose); durability supports 1-2x yearly dosing

Highly durable, dose dependent, serum Activin E reductions support dosing once or twice per year



Reductions in visceral and total fat mass with preservation of lean mass observed at three months



Left: Figure shows sample means and SEMs. All MMRM baseline and placebo comparisons from Day 8 onwards are p<0.003. Placebo includes one individual from 400 mg expansion. Green shading: >70% Activin E reductions in preclinical models led to fat loss; Right: All DEXA percentage changes and p-values are model-based, using the SAP pre-specified analysis; p-values are from tests of within-group change over time; no p values were statistically significant for placebo.

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

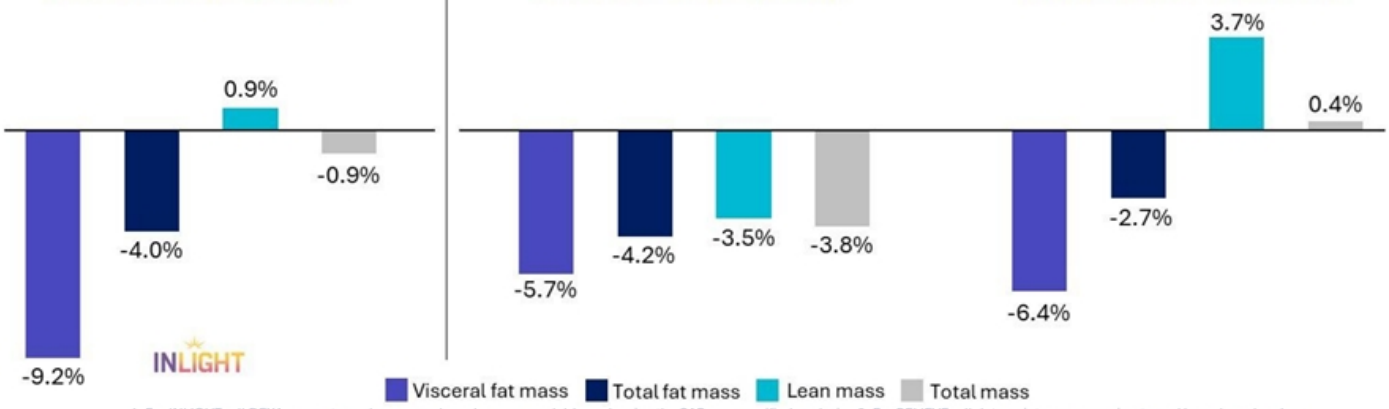
INLIGHT Phase 1 Trial
Placebo-adj. values at 12 weeks[1]

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

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

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

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



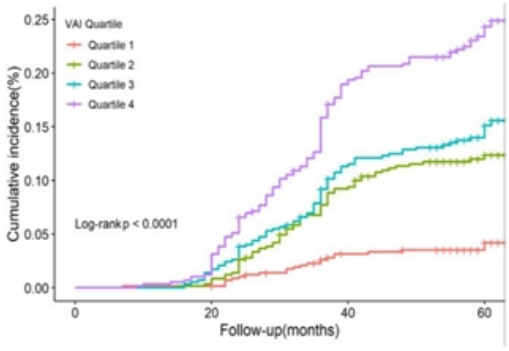
1. For INLIGHT, all DEXA percentage changes and p-values are model-based, using the SAP pre-specified analysis. 2. For BELIEVE, all data points are approximate and based on placebo-adjusted estimates extracted from figures, body weight reported as total mass, from Heymsfield SB, et al. Symposium – "*Can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

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

Visceral fat reduction is associated with multiple health benefits

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

Visceral fat increases risk of cardiovascular disease[5]



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

1. Gabriely et al., Diabetes 2002; Campos et al., Diabetes & Vascular Disease Research 2019; Huang et al., Front Endocrinol 2023. 2. Cesaro et al., Front Cardiovasc Med 2023; Khawaja et al., Curr Cardiol Rep 2024; Hiuge-Shimizu et al., J Atheroscler Thromb 2011. 3. Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020; ; Krittayaphong et al., Scientific Reports 2024; Hanlon & Yuan, Clin Liver Dis 2021. 4. Liao et al., PLoS ONE 2023; Jung et al., Endocrinol Metab 2020; Vilar-Gomez et al Gastroenterology 2015.. 5. Qaio et al. Cardiovasc Diabetol 21, 225 (2022). VAI = Visceral Adiposity Index

Potential to address more than one billion individuals with obesity globally

Monotherapy

Single agent in individuals living with obesity

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

Add-on

Combination with incretin treatments

- To leverage an orthogonal mechanism to incretins for enhanced efficacy

Maintenance

An off-ramp post-incretin treatments

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

Potentially transformational profile for treating obesity across multiple treatment settings

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

Near term anticipated updates for WVE-007

INLIGHT

1Q 2026

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

2Q 2026

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

1H 2026

Initiate Phase 2a MAD Portion

- In individuals with **higher BMI** and **comorbidities**

Expect to initiate new trials of WVE-007 as an add-on to incretin and as post-incretin maintenance in 2026

WVE-006
RNA editing (AIMer)

Alpha-1 antitrypsin deficiency (AATD)

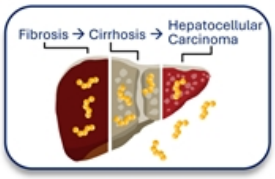
AATD impacts multiple organ systems and has limited treatment options

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

AATD Lung Disease

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

AATD Liver Disease



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

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

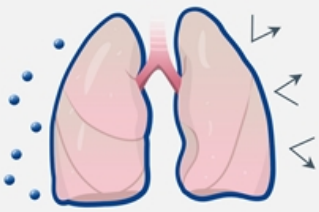
Strnad et al., 2020 *N Engl J Med* 382:1443-55; Blanco et al. 2017 *Int J Chron Obstruct Pulmon Dis* 12:561-69

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

WVE-006 (RNA editing)

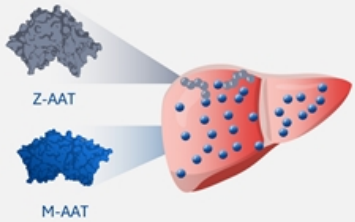
- Proprietary chemistry
- Highly specific (no bystanders)
- Subcutaneous delivery (GalNAc)
- Infrequent dosing

Restore circulating M-AAT and physiological AAT protein production



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

Reduce Z-AAT protein aggregation in liver



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

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

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

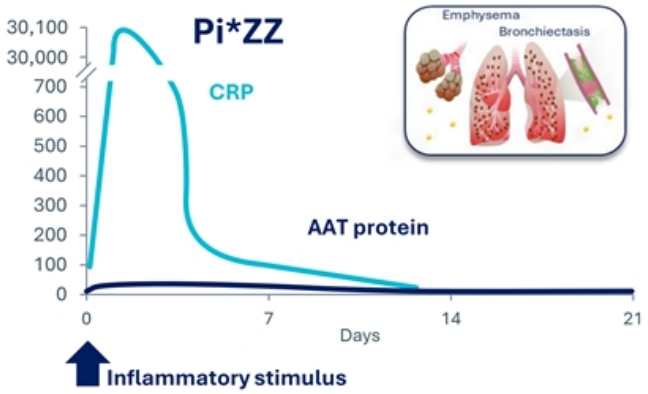
Genotype	Null	Pi*ZZ	Pi*MZ	Pi*MM
	No AAT protein	100% Z-AAT	Z-AAT and M-AAT	100% M-AAT
AAT levels increase during acute phase response	No	No	Yes	Yes
Risk of lung disease	Very high	High	Low	Normal
Risk of liver disease	None	High	Low	Normal

>50% RNA editing
> 11 µM AAT

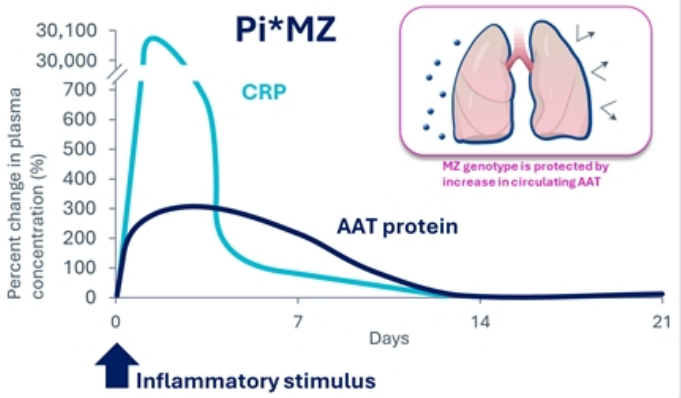
Goal: Shift Pi*ZZ individuals to AAT biomarker profile consistent with Pi*MZ genotype

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

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



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



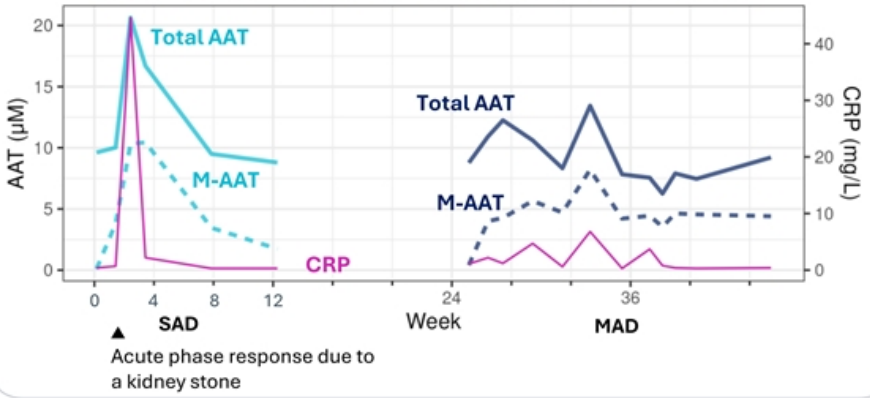
RNA editing has potential to restore dynamic AAT response to inflammation

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

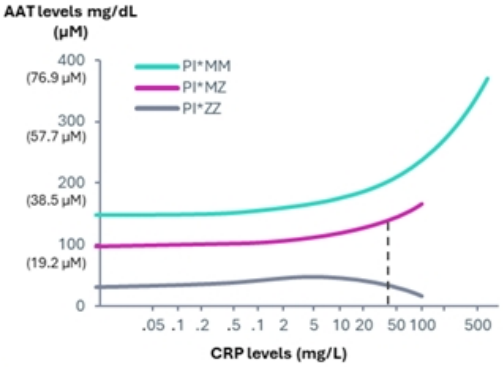
First-ever demonstration of ability to restore physiological serum AAT production; total AAT reached 20.6 µM during acute phase response

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

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



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



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

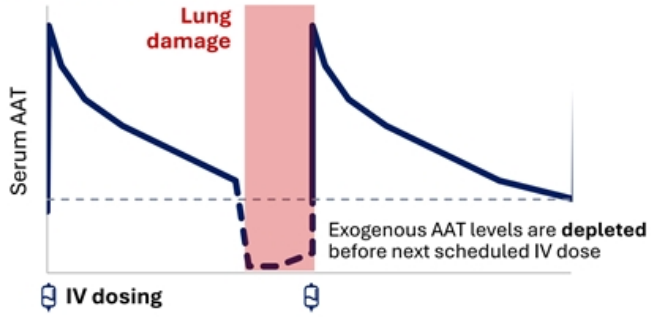
1 - Sanders et al., J COPD, 2018 CRP: C-reactive protein

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

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

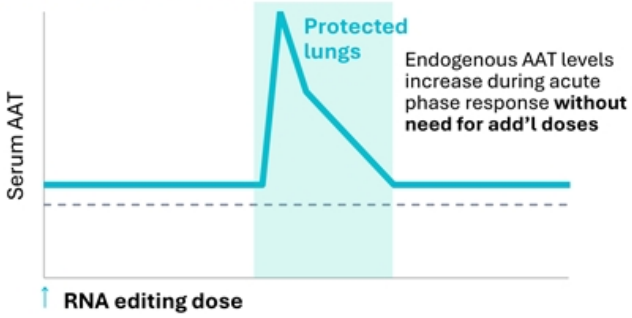
Illustrative model of impact of acute phase response

Augmentation therapy



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

WVE-006 treatment approach



- WVE-006 also reduces levels of Z-AAT

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

WVE-006 achieved key treatment goals of restoring MZ phenotype

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

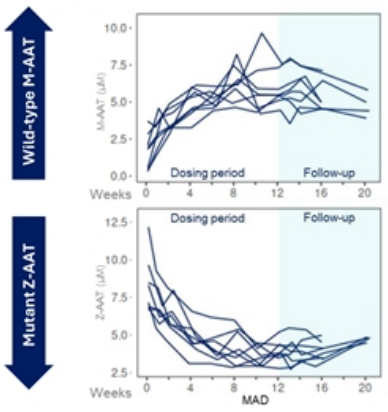
Plasma AAT of ~13 µM

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

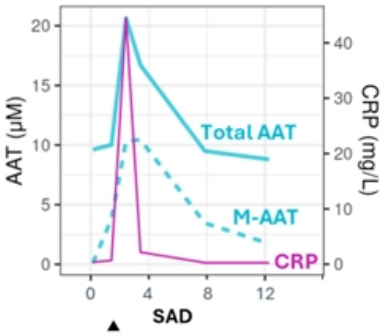
400 mg single dose
12.8 µM total AAT

200 mg multidose
11.9 µM total AAT

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



AAT reached >20 µM during an acute phase response



▲ Acute phase response due to a kidney stone

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

RestorAATion-2 clinical trial ongoing; 400 mg MAD data expected in 1Q 2026 and 600 mg SAD and MAD data expected in 2026

RESTORAATION

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

SAD → MAD Multi-dosing complete

SAD Cohort 3 600 mg	→	MAD Cohort 3 600 mg; Q4W
SAD Cohort 2 400 mg	→	MAD Cohort 2 400 mg; Q4W
SAD Cohort 1 200 mg	→	MAD Cohort 1 200 mg Q2W

Study key objectives

Safety and tolerability	Pharmacokinetics	Serum M-AAT levels

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

WVE-008
RNA editing (AIMer)

PNPLA3 I148M liver disease

WAVE LIFE SCIENCES

RNA editing program: WVE-008 (PNPLA3 AIMer) for liver disease

Clinically-validated RNA editing

- Efficient and consistent RNA editing
- Durable RNA editing supporting infrequent dosing
- Generally safe and well-tolerated

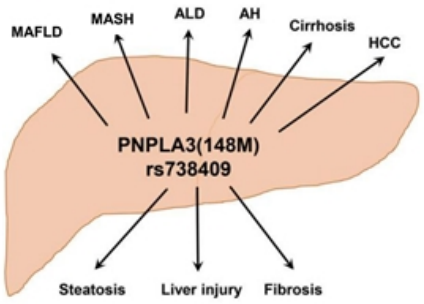
WVE-008 (PNPLA3)

- Strong foundation in human genetics
- Over nine million homozygous PNPLA3 I148M patients with liver disease in US and Europe
- GalNAc RNA editing approach uniquely aims to restore PNPLA3 function to fully address disease

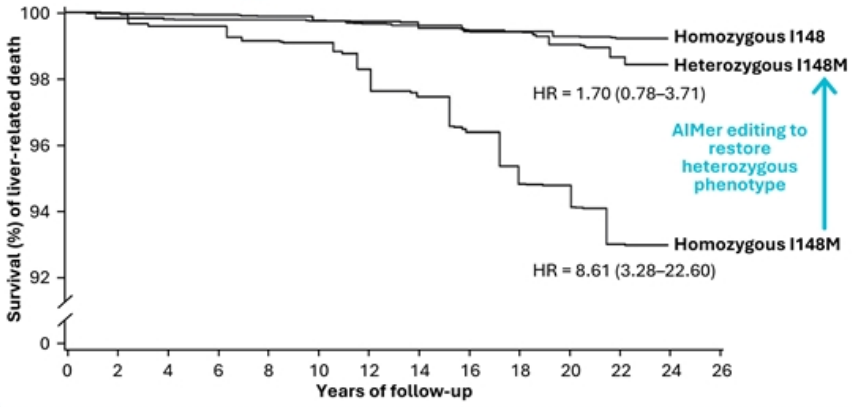
People homozygous for PNPLA3 I148M are at high risk for liver disease

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

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



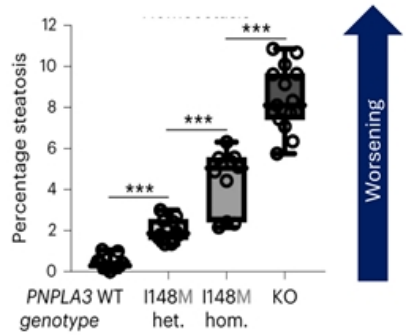
>50% RNA editing would support restoration of heterozygous phenotype with lower risk of liver complications and death

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

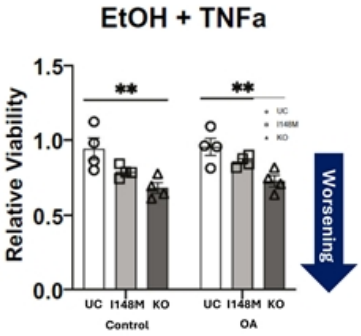
MAFLD, Metabolic dysfunction-associated fatty liver disease; MASH, Metabolic dysfunction-associated steatohepatitis; ALD, alcoholic liver disease; AH, Alcohol-associated hepatitis; HCC, hepatocellular carcinoma

Silencing of PNPLA3 in normal liver may worsen basal physiological functions

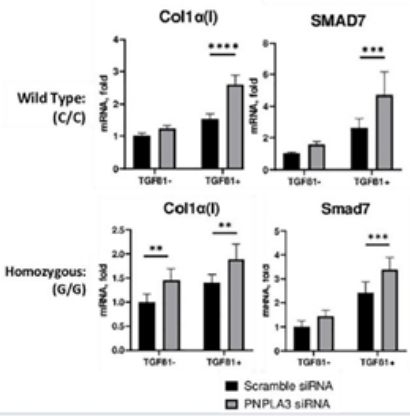
Silencing PNPLA3 worsens steatosis in iPSC-derived human liver organoids[2]



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



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



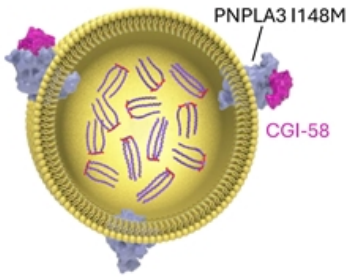
Functional PNPLA3 is imperative for liver health beyond improvements in steatosis

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

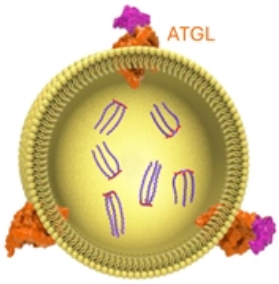
RNA editing approach

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



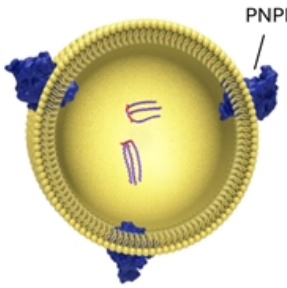
- PNPLA3 I148M accumulates on LDs, sequesters CGI-58, inhibits ATGL's lipase activity and lipid mobilization from ER
- Suppresses retinol metabolism in liver and worsens inflammation and fibrosis
- Promotes liver fat accumulation and fibrosis through activation of stellate cells

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



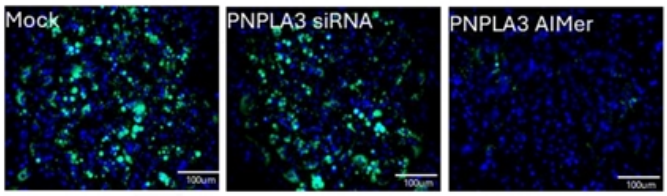
- Restores full PNPLA3 activity
- **Restores lipid mobilization, reverses steatosis, fibrosis, ballooning, and inflammation**

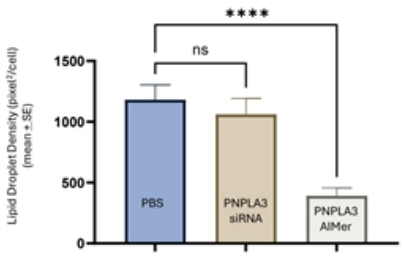
ATGL: adipose triglyceride lipase; CGI-58: co-factor for ATGL; ER endoplasmic reticulum; LDs: lipid droplets; CGI-58 also called ABHD5

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

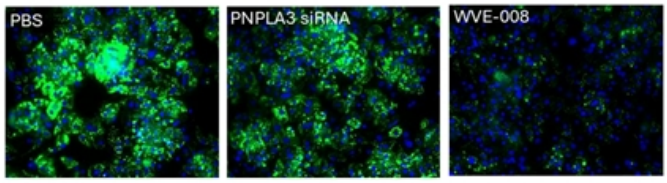
AIMers achieve efficient editing of PNPLA3, leading to reduction of liver fat

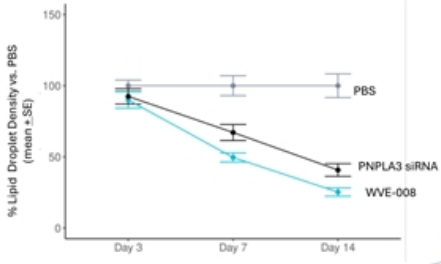
Significant decrease in liver fat with PNPLA3 editing in human HEPATOPAC® model with homozygous I148M





Decrease in liver fat with WVE-008 in monolayer model

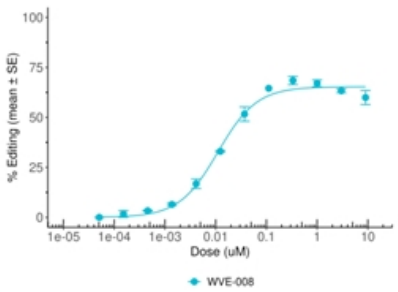




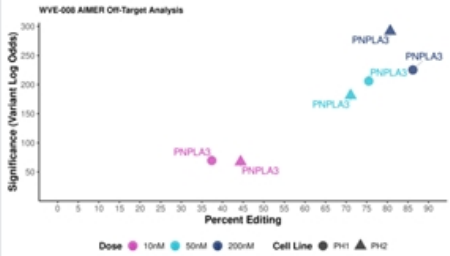
One-way ANOVA with Dunnett post hoc test comparisons to Mock **** P< 0.0001

WVE-008: Potential first-in-class, disease modifying therapy, for treatment of PNPLA3 I148M-driven liver disease

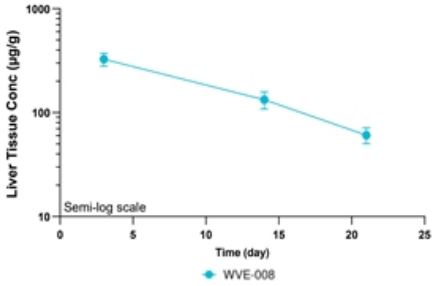
Potent editing with WVE-008



Highly specific editing with WVE-008



Tissue exposure supports excellent delivery



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

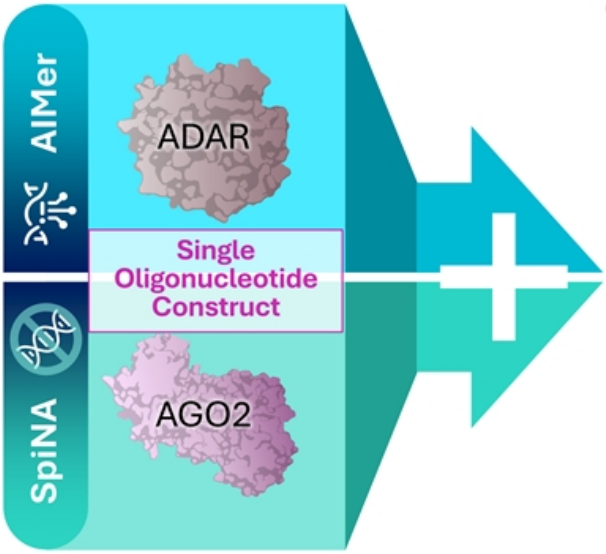
Left: 4-parameter log-logistic dose response curve; Middle: Analysis utilized RNA-sequencing with two separate primary human hepatocyte cell lines (PH1/2). Variant calling utilized GATK best practices for RNA variant calling using Mutect2 and display A->G evidence found when filtering for variants found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

Single oligonucleotide construct Bifunctional modality

Simultaneously knockdown and edit RNA

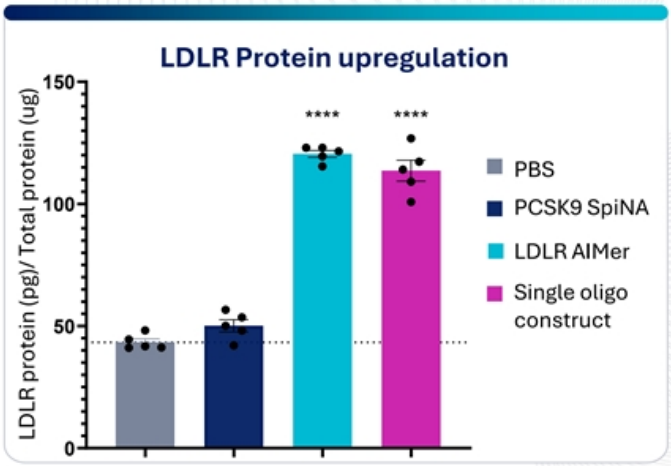
WAVE LIFE SCIENCES

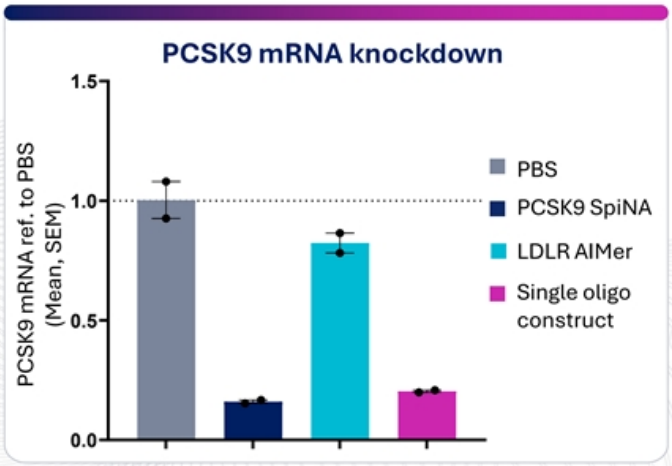
Reimagining RNA medicines: Bifunctional modality to simultaneously knockdown and edit RNA with single oligonucleotide construct



- ✓ Engage both endogenous Ago2 and ADAR enzymes
- ✓ 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

Single GalNAc-conjugated oligonucleotide construct can simultaneously upregulate and silence protein *in vitro*





Demonstrates potential to address complex indications that require engaging multiple targets

Primary human hepatocytes were treated in vitro with indicated compounds for 96 hours. Left: LDLR protein was measured using an ELISA; Stats: Welch's One-Way ANOVA with Dunnett's T3 post hoc-comparison. Right: PCKS9 transcript was measuring by qPCR using the ΔΔCt method

WVE-N531
Splicing

Duchenne muscular dystrophy

WAVE LIFE SCIENCES

Advancing WVE-N531 in exon 53 amenable DMD

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

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

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

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

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

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

NDA filing for accelerated approval with monthly dosing planned for 2026

Muscle content-adjusted dystrophin

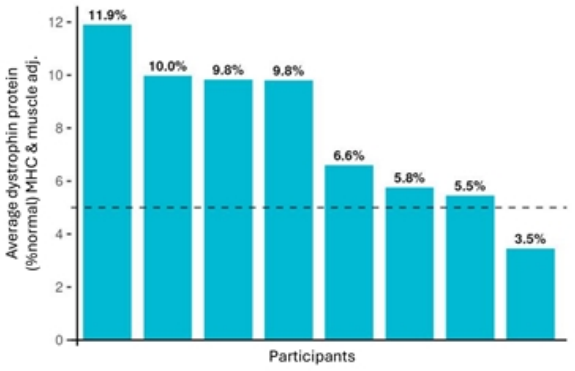
Potential best-in-class, consistent dystrophin expression

Potential best-in-class exon skipping and dystrophin

	Average: 24 and 48-week
Mean exon skipping induced	**54%** (95% CI: 46-63%)
Mean dystrophin expression[1]	**7.8%** (95% CI: 5.4-10.3%)

61-day tissue half-life supports monthly dosing

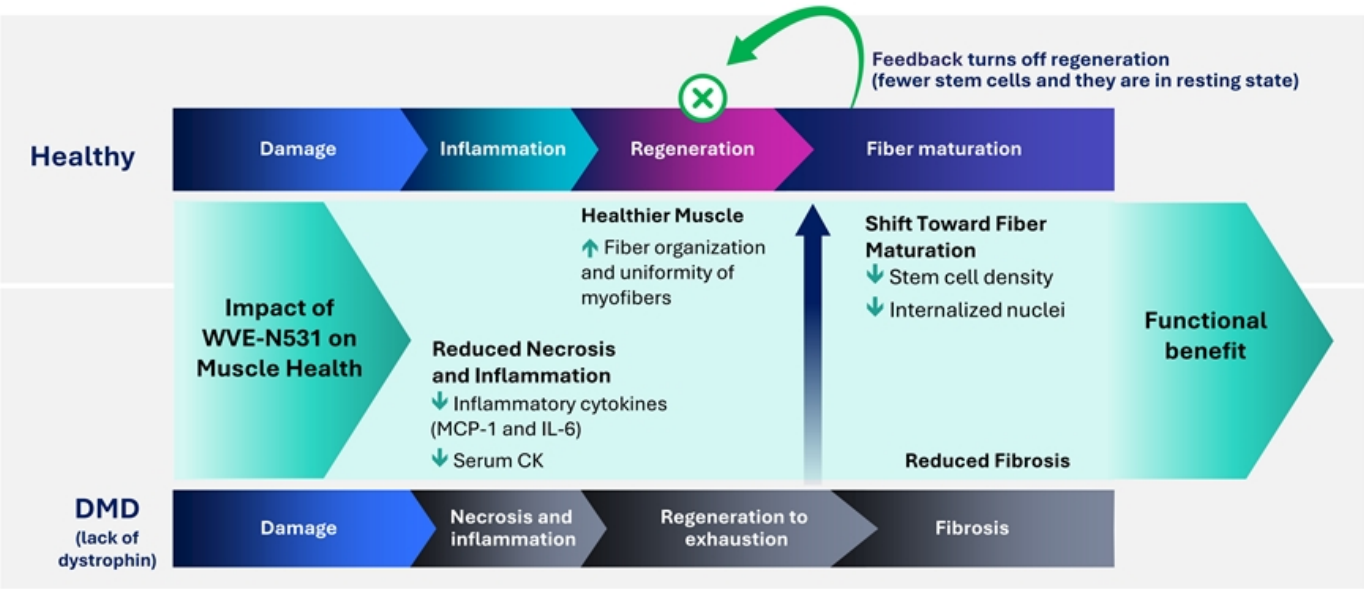
Consistently exceeded levels associated with milder Becker phenotype



88% of boys achieved greater than 5% average dystrophin

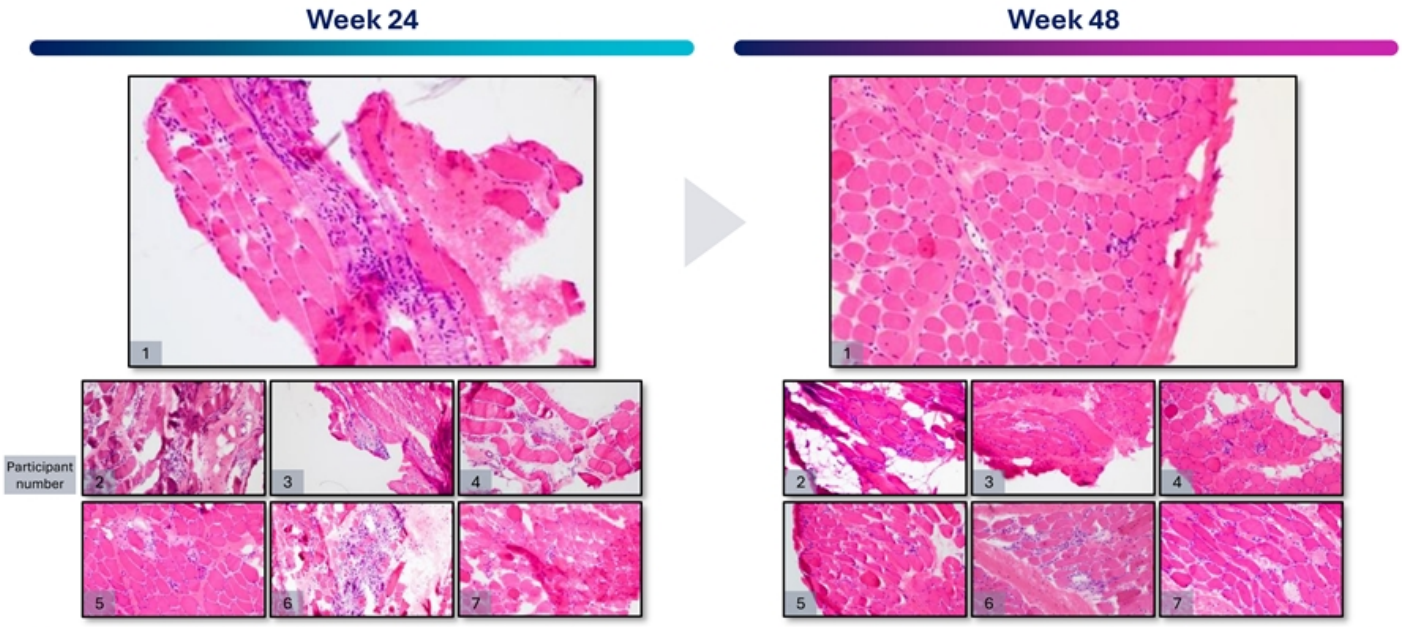
Left: 8 participants had muscle biopsies at week 24 and week 48, averages for these n=8 are summarized; Dystrophin measured by western blot (AB15277). Dystrophin expression was quantified from two isoforms; [1]MCA: muscle content-adjusted (MHC-normalized dystrophin/(total myofiber area/total area of biopsy section); Right: Average between 24 and 48 weeks.

WVE-N531 appears to shift dystrophic muscle towards healthy muscle



Cardone et al., 2023 Acta Neuropathol Comm

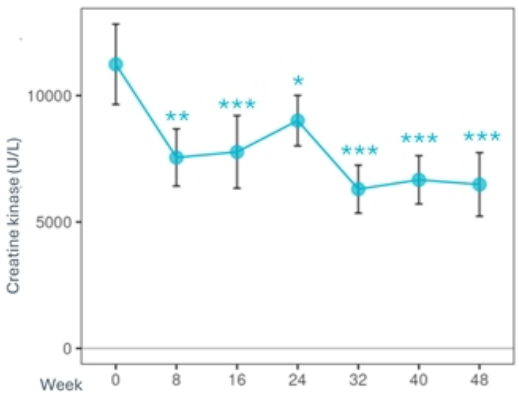
Evidence of reversal of fibrosis across majority of participants



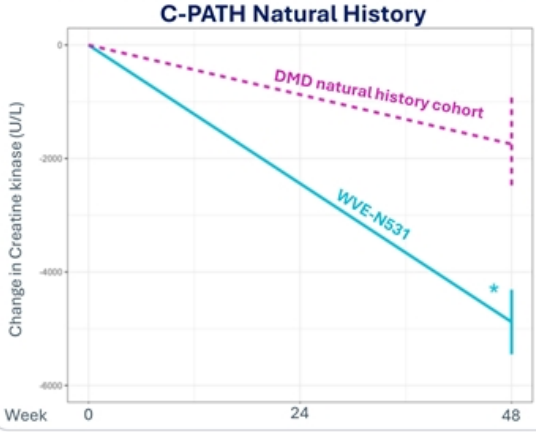
H&E-stained sections (20X magnification). Seven paired biopsies available from week 24 and 48 for histopathology.

Statistically significant reductions in creatine kinase (CK) as compared to baseline and natural history

~50% CK reduction from baseline at 48 weeks



Statistically significant reduction in CK vs. C-PATH Natural History

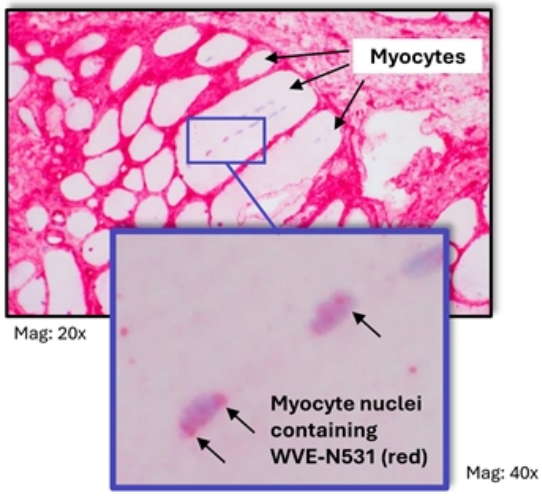


Decreased CK to levels observed in milder DMD individuals

*p<0.05, ** p<0.01, ***p<0.001; Data are mean ± SE
Left: n=11; right: n=10 (all ambulatory)

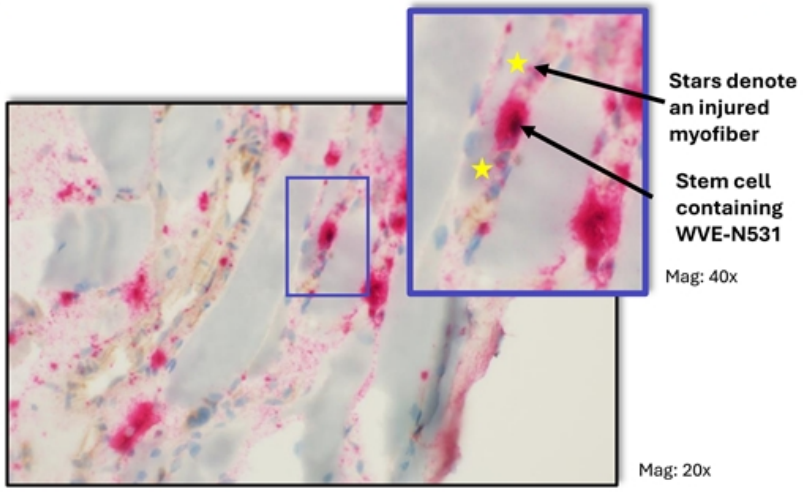
WVE-N531 is the only DMD therapeutic to show uptake in myogenic stem cells

WVE-N531 uptake in myofiber nuclei



In-situ hybridization for WVE-N531

WVE-N531 uptake in myogenic stem cells

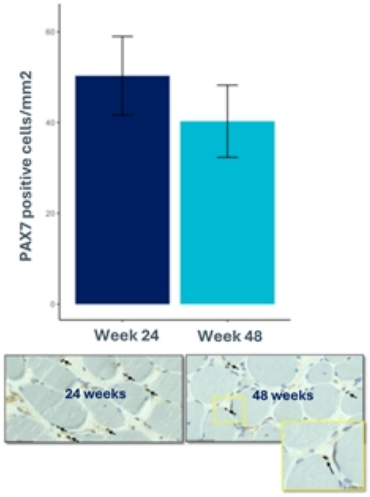


Dual staining utilizing in-situ hybridization for WVE-N531 and PAX7 immunohistochemistry for stem cells

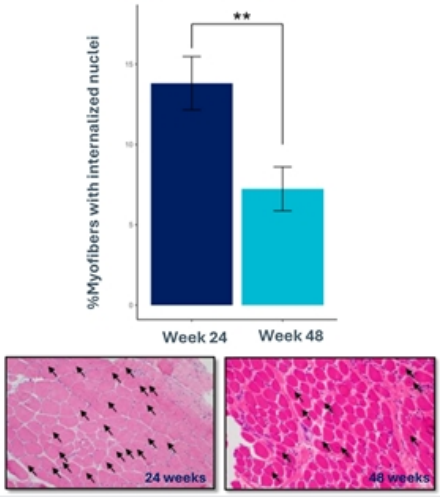
Changes to key cell populations in muscle and decrease in systemic inflammatory cytokines, suggesting transition to healthier muscle

Progression of regenerative to mature state of muscle tissue

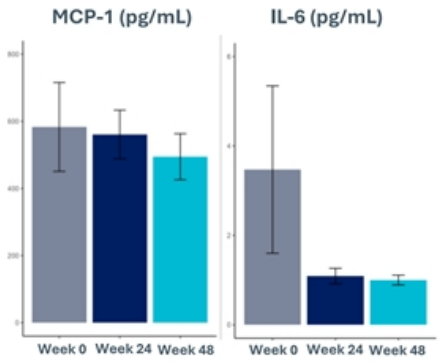
~20% change in density of myogenic stem cells at 48 weeks



Significant decrease (~48%) in internalized nuclei at 48 weeks



Decrease in serum MCP-1 and IL-6 suggests reduction in inflammation with treatment

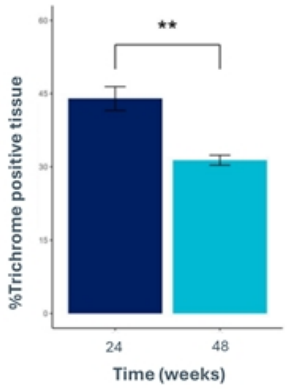


Left: NS; Data are mean ± SE (of n = 9); PAX7-positive cells/mm2 quantified using Pax7 immunohistochemistry (IHC) with HALO. Middle: **p<0.01 (two-tailed Welch's test); Data are mean ± SE; Internalized nuclei quantified using 6 random fields in H&E stained sections. Right: Data are means ± SE

First evidence of reversal of fibrosis with exon skipping treatment

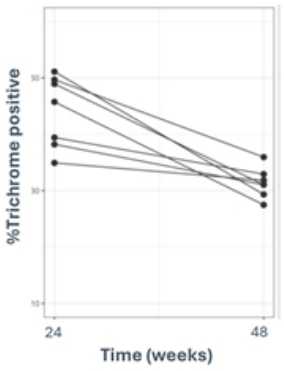
Mean fibrotic muscle declined 28.6% at 48W

(n = 7)

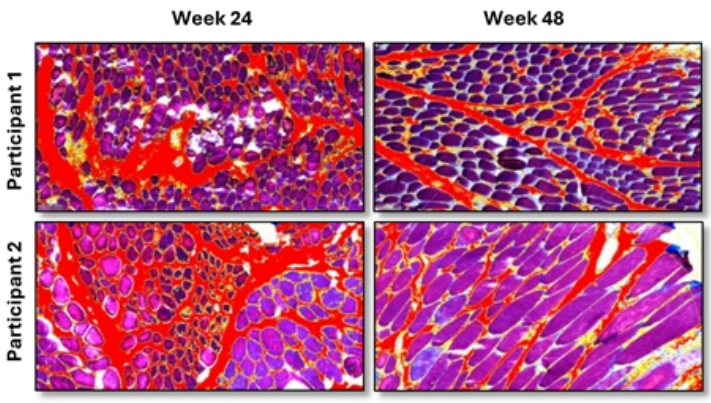


% Fibrotic muscle declined by individual

(n = 7)



Week 48 showed improved organization and uniformity of myofibers

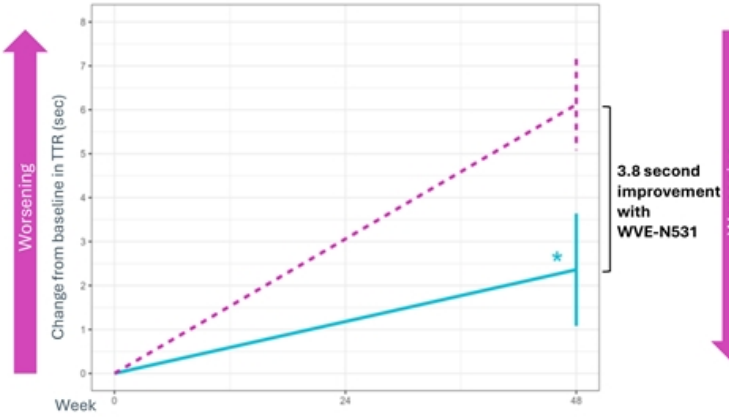


Right: Magnification 5X; fibrosis stained with trichrome stain and analyzed with HALO; ** p<0.01; Data are mean ± SE

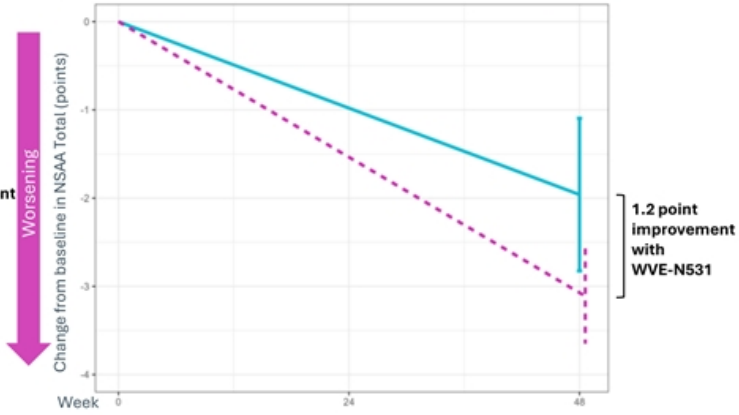
Statistically significant and clinically meaningful slowing of disease progression as measured by TTR

Functional benefits on other measures including NSAA

Mean change in time-to-rise (TTR)



Mean change in NSAA

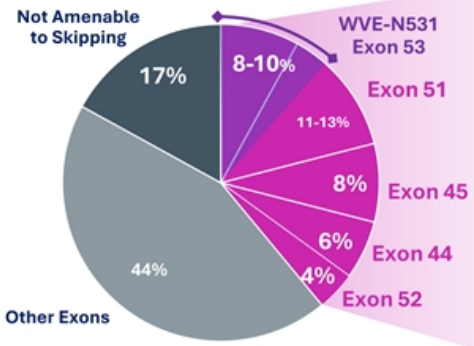


WAVE LIFE SCIENCES

Left: Minimal Clinical Important Difference (MCID) for TTR: 1.4 sec based on method from McDonald 2013; *p<0.05; Data are mean ± SE
Right: NSAA: North Star Ambulatory Assessment; data are mean ± SE

Wave DMD portfolio addresses >$2.4 billion opportunity in US alone with potential for expansion

Wave portfolio addresses up to 40% of the DMD population



Multiple drivers of value with Wave portfolio

Increasing exon skipping treatment rates

- ~40–50% of exon 53, 51, 45 skipping amenable boys remain untreated today
- No exon skipping therapies available for exons 44 and 52
- Advantages over gene therapy (endogenous dystrophin, favorable safety)

Switches from marketed exon skipping therapies

- Monthly dosing, superior dystrophin profile, and improvements in muscle health

Expansion to ex-US markets

- Potential best-in-class exon skipping profile where no exon skipping therapies are available

Aartsma-Rus, et al. 2009 Hum Mutat

WVE-003
Allele-selective silencing

Huntington's Disease

WAVE LIFE SCIENCES

Advancing WVE-003 to address HD across all stages of disease

WVE-003 is a first-in-class, allele-selective oligonucleotide for the treatment of HD

- HD is a monogenic autosomal dominant genetic disease; fully penetrant and affects entire brain
- No current disease modifying therapies for HD
- Characterized by cognitive decline, psychiatric illness, and chorea; ultimately fatal
- Expanded CAG triplet repeat in *HTT* gene results in production of mutant huntingtin protein (mHTT) and loss of function of wild-type huntingtin protein (wtHTT)

>200,000 patients with HD across all disease states

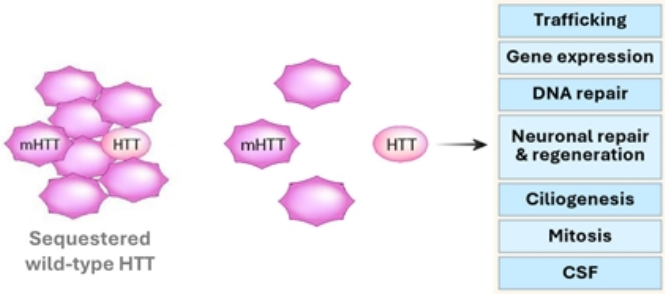
Pre-Symptomatic HD	Symptomatic HD
(~160K in US and Europe)	(~65K in US and Europe)

Sources on wtHTT: 1. Leavitt 2006 2. Cattaneo 2005 3. Kumar 2016 4. Franco-Iborra 2020 5. Hamilton 2015 6. Ochaba 2014 7. Wong 2014 8. Rui 2015 9. Caviston 2007 10. Twelvetrees 2010 11. Strehlow 2007 12. Milnerwood 2010 13. Smith-Dijak 2019 14. Tousley 2019 15. Zhang 2018 16. McAdam 2020 17. Altar 1997 18. Zuccato 2001 19. Gauthier 2004 20. Ferrer 2000 21. Baquet 2004 22. Liu 2011 23. Karam 2015

Wild-type HTT (wtHTT) is critical for normal neuronal function and loss of wtHTT contributes to cellular dysfunction

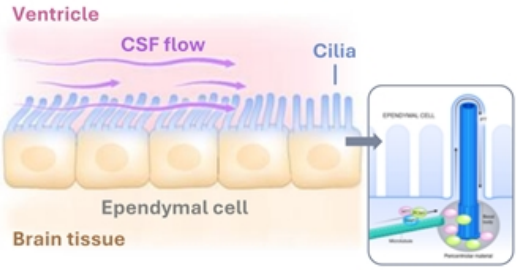
Mutant HTT has a detrimental effect on wild-type HTT function

- Lowering mHTT is expected to restore physiological control over HTT gene expression and relieve its detrimental effect on wtHTT function



Wild-type HTT is crucial for cilia health

- In the absence of wtHTT, ciliogenesis fails, disrupting CSF flow, causing hydrocephalus



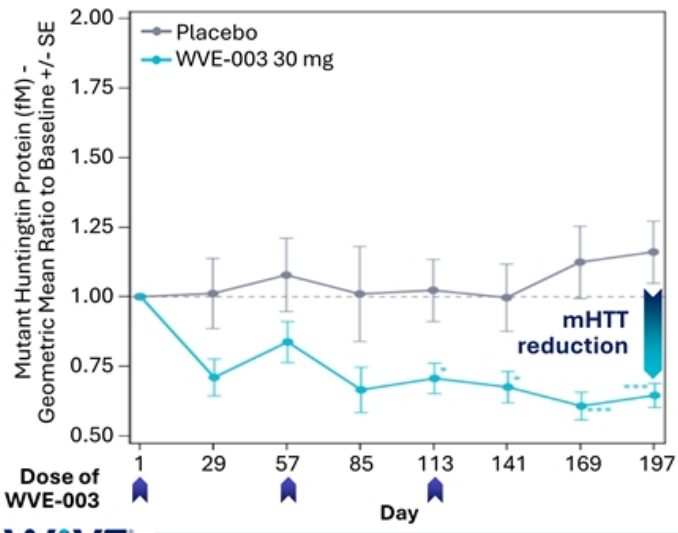
Only an allele-selective approach can ameliorate both loss-of-function and gain-of-function disruptions driven by mHTT

Saudou & Humbert 2016 Neuron; Cason et al., 2022 Nat Rev Cell Biol; Laundos et al., 2023 Front Cell Dev Biol; Kaliszewski et al., 2015 Cell Death Diff; Keryer et al., 2011 J Clin Invest Khoshnan & Patterson, 2011. Neurobiol Dis; Pogoda et al., 2021 Curr Med Chem; Hsiao et al., 2013 Hum Mol Genet

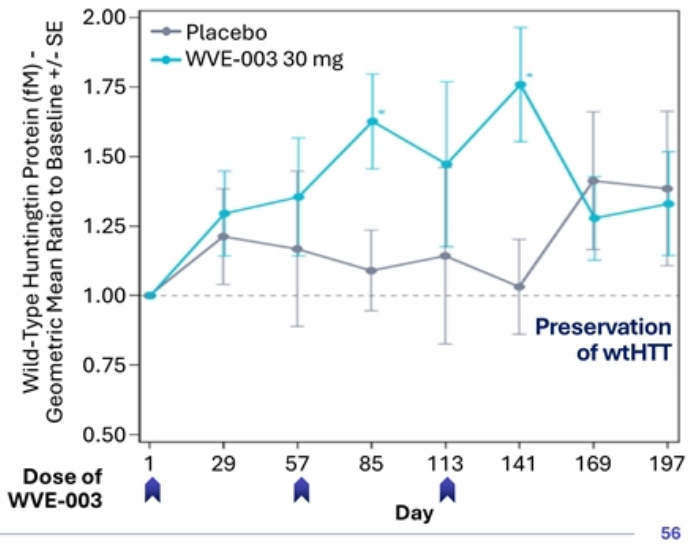
Allele-selective CSF lowering of mutant HTT protein of up to an industry leading 46% with three doses of WVE-003 and preservation of wild-type HTT

Durability of mHTT reductions supports potential for quarterly dosing intervals

Mutant HTT protein levels in CSF



Wild-type HTT protein levels in CSF



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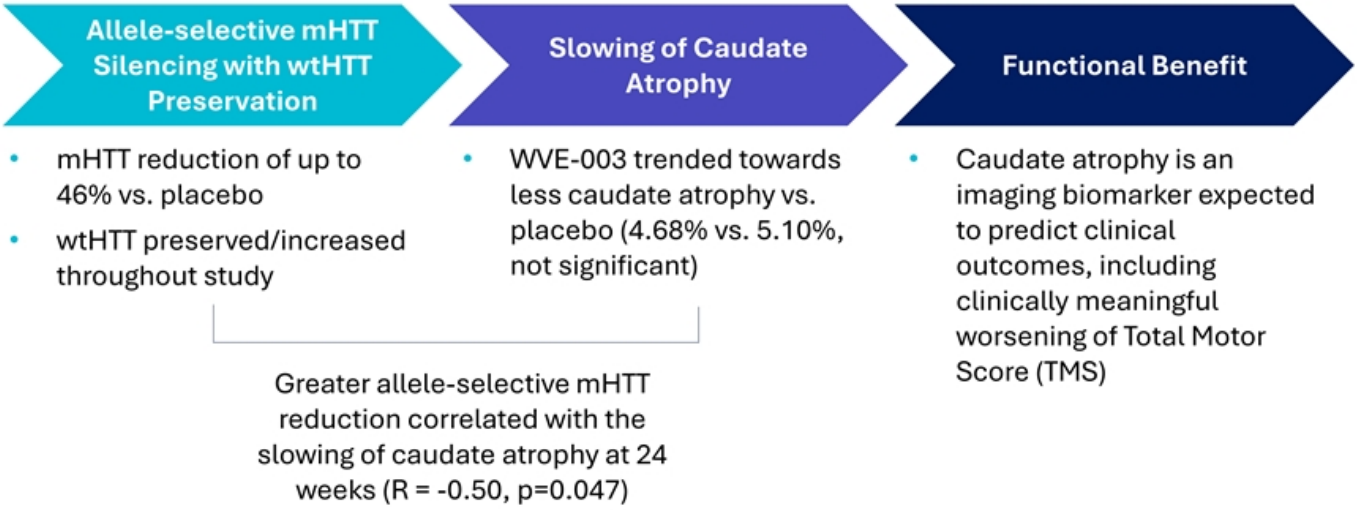
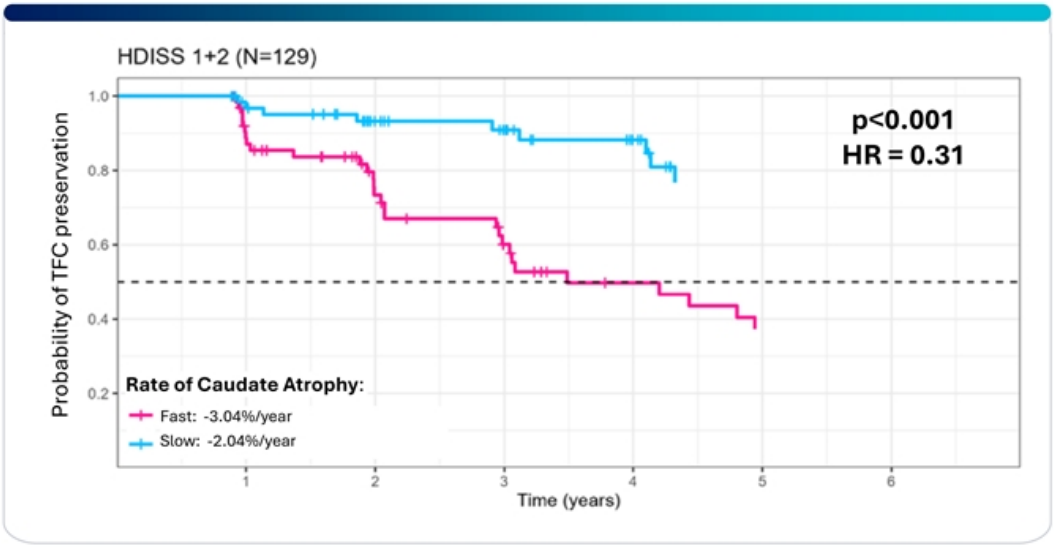
* p<0.05, **p<0.01, ***p<0.001, ****p<0.0001
mHTT: mutant huntingtin protein; wtHTT: wild-type huntingtin protein
From June 25, 2024 SELECT-HD disclosure

WVE-003 leads to allele-selective mHTT reduction, correlating with slowing of caudate atrophy



Liu et al., 2023 Brain Comm

Analysis of natural history demonstrates that absolute reduction of 1% in rate of caudate atrophy is associated with delay of onset of disability by ≥7.5-years



Wave internal analysis; TRACK-HD and PREDICT-HD are longitudinal HD natural history studies that include MRI brain imaging, clinical outcome assessments. Paulson et al., Neurosci.2014, Tabrizi et al., Lancet Neurol 2009, Tabrizi et al., Lancet Neurol 2012, Tabrizi et al., Lancet Neurol. 2013
TFC: Total Functional Capacity

Reimagining RNA medicines

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

Anticipated upcoming milestones

RNAi	**WVE-007** *(INHBE)* *Obesity*	**1Q 2026:** Deliver 3-month 400 mg data and 6-month 240 mg data **2Q 2026:** Deliver 3-month 600 mg data and 6-month 400 mg data **1H 2026:** Initiate Phase 2a multidose portion of INLIGHT in individuals living with obesity with higher BMI and comorbidities **2026:** Initiate new trials evaluating WVE-007 as an add-on to incretin and as post-incretin maintenance
RNA editing	**WVE-006** *AATD*	**1Q 2026:** Deliver data from 400 mg multidose cohort **2026:** Deliver single and multidose data from 600 mg cohort
	WVE-008 *Liver disease*	**2026:** File CTA for WVE-008
Splicing	**WVE-N531** *(Exon 53)* *DMD*	**2026:** Submit NDA to support accelerated approval of WVE-N531 with monthly dosing
Antisense	**WVE-003** *(SNP3)* *HD*	Submit IND application for potentially registrational Phase 2/3 study of WVE-003 in conjunction with prospective strategic partner

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CTA: Clinical Trial Application; NDA: New Drug Application; IND: Investigational New Drug


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