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): August 8, 2024

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 August 8, 2024, Wave Life Sciences Ltd. (the "Company") announced its financial results for the quarter ended June 30, 2024. 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 August 8, 2024, 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 August 8, 2024
99.2	Corporate Presentation of Wave Life Sciences Ltd. dated August 8, 2024
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: August 8, 2024

Wave Life Sciences Reports Second Quarter 2024 Financial Results and Provides Business Update

Successful clinical translation of Wave's RNA medicines platform in HD patients with WVE-003 provides further validation of Wave's proprietary platform with PN and stereochemistry; opt-in package for WVE-003 submitted to partner Takeda and engagement with regulators initiated to discuss potential path to accelerated approval

Dystrophin data on track for 3Q 2024 from potentially registrational FORWARD-53 trial of WVE-N531, which has previously demonstrated industry-leading exon skipping of 53%; positive data would unlock a best-in-class functional dystrophin franchise for DMD

Dosing initiated in 3Q 2024 in RestorAATion-2 clinical trial of WVE-006 in AATD patients; proof-of-mechanism data in AATD patients expected in 4Q 2024

New preclinical data supporting INHBE siRNA (WVE-007) as a potential best-in-class treatment for obesity, as well as new data from Wave's wholly owned pipeline of RNA medicines, expected at R&D Day in Fall 2024

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

CAMBRIDGE, Mass., August 8, 2024 – 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, 2024, and provided a business update.

"With our recent positive SELECT-HD trial results, we have further validated our chemistry and the clinical translation of our platform. Today, we have built an RNA medicines platform that is positioned to sustainably translate clinical genetic insights into transformational medicines as we continue to advance our lead programs through multiple important milestones in the second half of this year," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Clinical results from our SELECT-HD trial in HD demonstrated statistically significant, potent, and durable allele-selective silencing with WVE-003, and we are working rapidly to engage regulators on a potential path to accelerated approval. These data have also bolstered our confidence ahead of expected upcoming readouts from our potentially registrational FORWARD-53 trial in DMD and our RestorAATion-2 trial in AATD. In parallel with these efforts, we continue to drive our best-in-class obesity candidate, WVE-007, toward the clinic and are on track to initiate the first-in-human study in the first quarter of next year. We look forward to providing additional updates on our growing, high-value pipeline and our progress towards reimagining what's possible for human health at our R&D Day this Fall."

Recent Business Highlights

HD (allele-selective silencing)

- **WVE-003** is a first-in-class, allele-selective oligonucleotide designed to lower mutant huntingtin (mHTT) protein and preserve healthy, wild-type huntingtin (wtHTT) protein, a protein critical to the health of the central nervous system. As compared to non-selective HTT lowering approaches, WVE-003 is uniquely positioned to address presymptomatic HD patients, as well as symptomatic patients. There are currently no disease modifying therapies for HD, which affects over 200,000 individuals across pre-symptomatic and symptomatic disease stages in the US and Europe. WVE-003 is expected to address approximately 40% of the HD population, and up to 80% of HD patients may be addressed in the future with other SNP-targeted candidates.
- In June, Wave announced positive clinical data from the Phase 1b/2a SELECT-HD study of WVE-003. Results from the multi-dose (three doses every eight weeks) portion showed clear translation of target engagement to clinic with statistically significant, potent, durable and allele-selective reductions in CSF mHTT of up to 46% and preservation of healthy protein. This cohort also revealed a statistically significant correlation between mHTT reductions and slowing of caudate atrophy, indicating a potential benefit of allele-selective mHTT reductions. Structural brain MRI changes, such as caudate atrophy, are well-characterized measures of disease progression and neurodegeneration in HD. WVE-003 was generally safe and well-tolerated, with mild-to-moderate adverse events and no Serious Adverse Events.
- Wave has submitted its opt-in package to its partner, Takeda, and initiated engagement with regulators on a clinical development path to accelerated approval.
- **Expected upcoming milestone:** Wave expects a decision from Takeda on their option right, as well as feedback from regulators on a clinical development path to accelerated approval by year-end.

DMD (exon skipping)

- **WVE-N531** is an exon-skipping oligonucleotide designed to induce production of endogenous, functional dystrophin protein for the treatment of boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. In a previously completed study (three doses every other week), WVE-N531 achieved industry-leading mean exon skipping levels of 53%, mean muscle tissue concentrations of ~42,000 ng/g, and distribution to myogenic stem cells (also known as satellite cells) in all study participants.
- Wave continues to advance FORWARD-53, a potentially registrational, open-label clinical trial of 11 boys with DMD, which is evaluating WVE-N531 administered every-other-week. Endpoints include dystrophin expression after 24 and 48 weeks of treatment, as well as pharmacokinetic, safety and tolerability data.
- Pending positive results from the FORWARD-53 trial, the company is planning to advance a broader DMD pipeline of PN-modified oligonucleotides for skipping other exons, with the goal of providing new and best-in-class treatment options for a larger population of boys with DMD.
- In 2023, exon skipping therapeutics for DMD achieved approximately ~$1 billion in sales, primarily in the US, across exons covering approximately ~29% of the DMD population. WVE-N531 could address up to 10% of the DMD population, which encompasses over 2,000 boys in the US and Europe; and with the addition of other exons, Wave could address up to 40% of the DMD population.
- **Expected upcoming milestone:** Wave expects to deliver data, including dystrophin protein expression from muscle biopsies after 24 weeks of treatment, in the third quarter of 2024.

AATD (GalNAc-RNA editing)

- **WVE-006** is a GalNAc-conjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that is uniquely designed to address AATD-related lung disease, liver disease, or both. WVE-006 does not use a lipid-nanoparticle (LNP) delivery system. WVE-006 is currently being evaluated in the RestorAATion-2 Phase 1b/2a study in Pi*ZZ patients with AATD.
- There are an estimated 200,000 Pi*ZZ patients in the US and Europe. Treatment options are currently limited to weekly IV augmentation therapy for lung disease only (representing over $1 billion in world-wide sales in 2023). There are no approved therapies to address AATD liver disease, which ultimately requires many patients to undergo liver transplantation.
- In the third quarter of 2024, Wave initiated dosing in the single dose portion of the first dose cohort of RestorAATion-2, at a dose level expected to engage target, meaning inducing RNA editing, based on preclinical data.
- **Expected upcoming milestone:** Wave expects to deliver proof-of-mechanism data from RestorAATion-2 in patients with AATD in the fourth quarter of 2024.

Obesity (GalNAc-siRNA)

- **WVE-007** is a GalNAc-conjugated small interfering RNA (GalNAc-siRNA) that is designed to silence the INHBE (Inhibin ßE) gene to induce lipolysis (fat-burning) while preserving muscle mass to restore and maintain a healthy metabolic profile thereby recapitulating the protective effects of INHBE loss-of-function (LoF) mutations. Heterozygous INHBE LoF carriers, identified through multiple large human genetic databases including UK Biobank, have a favorable cardiometabolic profile, including reduced abdominal obesity and reduced odds of type 2 diabetes and coronary artery disease.
- WVE-007 has potential to address obesity as a front-line monotherapy, in combination with GLP-1s for further improvement of weight loss or to reduce the doses of GLP-1s, or as a maintenance therapy following cessation of GLP-1s.
- In preclinical mouse models, Wave's INHBE GalNAc-siRNA has demonstrated highly potent (ED50 < 1mg/kg) and durable silencing following one, low-single-digit dose, supporting every-six-month or annual subcutaneous dosing in humans. Preclinical data also demonstrated weight loss similar to semaglutide, with no loss of muscle mass and a reduction in fat mass with preferential effects on visceral fat, consistent with the profile of INHBE LoF carriers in human genetics.
- In a separate ongoing study in DIO mice, when administered in combination with semaglutide, a single dose of Wave's INHBE GalNAc-siRNA doubled the weight loss observed with semaglutide alone and this effect was sustained throughout the duration of the study. As previously reported, treatment with Wave's INHBE GalNAc-siRNA upon cessation of semaglutide treatment curtailed expected rebound weight gain. The company plans to share additional preclinical data later this year.
- **Expected upcoming milestone:** Wave expects to initiate a clinical trial for WVE-007 in the first quarter of 2025.

RNA Medicines Platform and Pipeline Expansion

- Wave plans to hold an R&D Day in Fall 2024 which will highlight its innovations in chemistry and pipeline of transformative RNA medicines, as well as new preclinical data from Wave's wholly owned portfolio of candidates, including WVE-007 (INHBE siRNA).
- Wave continues to advance its pipeline of wholly owned RNA therapeutics across a range of high-impact GalNAc-hepatic and extra-hepatic targets. Powered by genetic datasets and deep learning models, Wave is also utilizing its proprietary "edit-verse" to identify new RNA editing targets that leverage easily accessible biomarkers, offer efficient paths to proof-of-concept in humans, address diseases of high unmet need, and represent meaningful commercial opportunities.

Financial Highlights

- Cash and cash equivalents were $154.0 million as of June 30, 2024, compared to $200.4 million as of December 31, 2023. Wave expects that its current cash and cash equivalents will be sufficient to fund operations into the fourth quarter of 2025. Potential future milestone and other payments to Wave under its GSK and Takeda collaborations are not included in its cash runway.
- Revenue was $19.7 million for the second quarter of 2024, as compared to $22.1 million in the second quarter of 2023.
- Research and development expenses were $40.4 million in the second quarter of 2024, as compared to $33.3 million in the second quarter of 2023. General and administrative expenses were $14.3 million in the second quarter of 2024, as compared to $12.3 million in the second quarter of 2023.
- Net loss was $32.9 million for the second quarter of 2024, as compared to $21.1 million for the second quarter of 2023.

Investor Conference Call and Webcast

Wave will host an investor conference call today at 8:30 a.m. ET to review the second quarter 2024 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 following audio-conferencing link: available here. Once registered, participants will receive the dial-in information. 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 RNA medicines platform, PRISM®, combines multiple modalities, chemistry innovation and deep insights in human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Its toolkit of RNA-targeting modalities includes editing, splicing, RNA interference 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 Duchenne muscular dystrophy, Alpha-1 antitrypsin deficiency and Huntington's disease, as well as a preclinical program in obesity. 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 (formerly Twitter) 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, site activation, patient recruitment, patient enrollment, dosing, generation and reporting of data and completion of our clinical trials, including interactions with regulators and any potential registration based on these data, and the timing and announcement of such events; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; our expectations with respect to how our clinical data successes to date may predict success for our future therapeutic candidates, future clinical data readouts and further

validate of our platform; ongoing and future preclinical activities and programs; regulatory submissions and timing for regulatory feedback; the progress and potential benefits of our collaborations; the potential achievement of milestones under our collaborations and receipt of cash payments therefor; the potential of our preclinical data to predict the behavior of our compounds in humans; our identification and expected timing of future product candidates and their therapeutic potential; the anticipated benefits of our therapeutic candidates and pipeline compared to our competitors; patient population estimates related to our therapeutic candidates; our ability to design compounds using various modalities and the anticipated benefits of that approach; the breadth and versatility of our PRISM drug discovery and development platform; the expected benefits of our stereopure oligonucleotides compared with stereorandom oligonucleotides; the potential benefits of our RNA editing capability, including our AIMers, compared to others; the potential for certain of our programs to be best-in-class or first-in-class; the potential benefits of WVE-007, and the potential areas where we may be able to address obesity with WVE-007; the potential benefits that our "edit-verse" may provide us, including identifying new RNA editing targets; the status and progress of our programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; the benefits of RNA medicines generally; the strength of our intellectual property and the data that support our IP; 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. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the following: our ability to finance our drug discovery and development efforts and to raise additional capital when needed; the ability of our preclinical programs to produce data sufficient to support our clinical trial applications and the timing thereof; the clinical results of our programs and the timing thereof, which may not support further development of our product candidates; actions of regulatory authorities and their receptiveness to our adaptive trial designs and accelerated approval pathways, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing regulatory interactions and future clinical trials; the effectiveness of PRISM; the effectiveness of our RNA editing capability and our AIMers; our ability to demonstrate the therapeutic benefits of our candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our dependence on third parties, including contract research organizations, contract manufacturing organizations, collaborators and partners; our ability to manufacture or contract with third parties to manufacture drug material to support our programs and growth; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for the indications we are pursuing; our ability to maintain the company infrastructure and personnel needed to achieve our goals; and the information under the caption "Risk Factors" contained in our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and in other filings we make with the SEC from time to time. We undertake no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	June 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 153,958	$ 200,351
Accounts receivable	1,290	21,086
Prepaid expenses	12,147	9,912
Other current assets	4,680	4,024
Total current assets	172,075	235,373
Long-term assets:		
Property and equipment, net of accumulated depreciation of $44,459 and $42,709 as of June 30, 2024 and December 31, 2023, respectively	11,783	13,084
Operating lease right-of-use assets	20,329	22,637
Restricted cash	3,731	3,699
Other assets	900	156
Total long-term assets	36,743	39,576
Total assets	$ 208,818	$ 274,949
Liabilities, Series A preferred shares, and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 18,149	$ 12,839
Accrued expenses and other current liabilities	10,677	16,828
Current portion of deferred revenue	137,138	150,059
Current portion of operating lease liability	7,164	6,714
Total current liabilities	173,128	186,440
Long-term liabilities:		
Deferred revenue, net of current portion	9,582	15,601
Operating lease liability, net of current portion	21,711	25,404
Total long-term liabilities	31,293	41,005
Total liabilities	$ 204,421	$ 227,445
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at June 30, 2024 and December 31, 2023	$ 7,874	$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 122,479,289 and 119,162,234 shares issued and outstanding at June 30, 2024 and December 31, 2023, respectively	$ 950,530	$ 935,367
Additional paid-in capital	135,603	129,237
Accumulated other comprehensive loss	(279)	(124)
Accumulated deficit	(1,089,331)	(1,024,850)
Total shareholders' equity (deficit)	$ (3,477)	$ 39,630
Total liabilities, Series A preferred shares, and shareholders' equity (deficit)	$ 208,818	$ 274,949

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,	
	2024	2023	2024	2023
Revenue	$ 19,692	$ 22,106	$ 32,230	$ 35,035
Operating expenses:				
Research and development	40,393	33,314	73,840	64,293
General and administrative	14,296	12,265	27,845	24,500
Total operating expenses	54,689	45,579	101,685	88,793
Loss from operations	(34,997)	(23,473)	(69,455)	(53,758)
Other income, net:				
Dividend income and interest income	2,092	2,251	4,627	4,124
Other income (expense), net	(18)	118	347	1,125
Total other income, net	2,074	2,369	4,974	5,249
Loss before income taxes	(32,923)	(21,104)	(64,481)	(48,509)
Income tax benefit (provision)	—	—	—	—
Net loss	$ (32,923)	$ (21,104)	$ (64,481)	$ (48,509)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.25)	$ (0.20)	$ (0.50)	$ (0.47)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	129,527,003	105,462,414	129,399,340	103,768,971
Other comprehensive loss:				
Net loss	$ (32,923)	$ (21,104)	$ (64,481)	$ (48,509)
Foreign currency translation	(81)	(100)	(155)	(121)
Comprehensive loss	$ (33,004)	$ (21,204)	$ (64,636)	$ (48,630)

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Exhibit 99.2

Wave Life Sciences

Corporate Presentation

August 8, 2024

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.

Building a leading RNA medicines company

Novel RNA medicines platform (PRISM®)

- Multi-modal: RNA editing, RNAi, splicing, allele-selective silencing
- Best-in-class, clinically-validated oligonucleotide chemistry (PN, stereochemistry)

Differentiated RNA medicines pipeline

WVE-006 in AATD

WVE-007 in Obesity

WVE-N531 in DMD

WVE-003 in HD

Strategic collaborations (GSK and Takeda) | **In-house GMP manufacturing** | **Strong and broad IP**

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

PRISM platform: Unlocking the broad potential of RNA medicines

Wave is uniquely positioned to harness human genetic insights and biological machinery in our body to deliver powerful ways to treat both rare and prevalent human diseases

Deep genetic insights

Leveraging **propriety machine learning models**, as well as accessing **UK Biobank** and other **large human genetic databases**

Multi-modal platform

Therapeutic candidates **harness endogenous enzymes** to optimally address disease biology

- RNA editing
- RNAi
- Splicing
- Antisense allele-selective silencing

Best-in-class, stereopure therapeutics

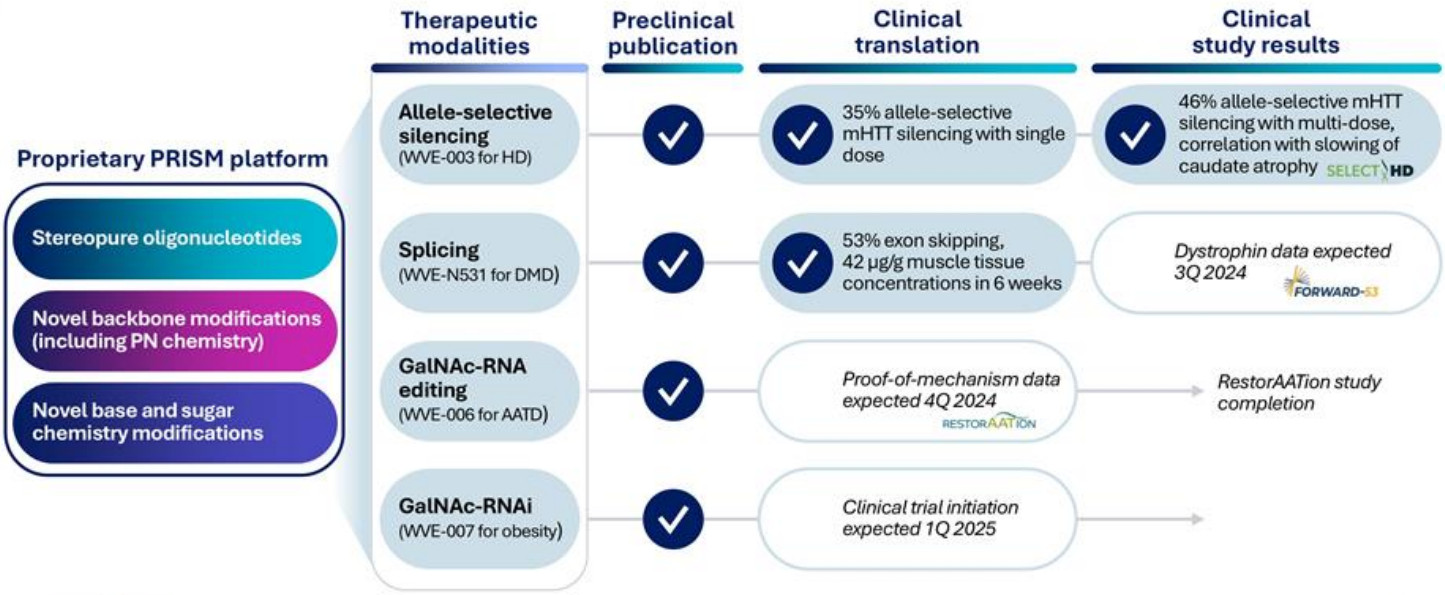
Best-in-class, rationally designed oligonucleotides enabled by **proprietary, clinically-validated** chemistry, including **PN** and **stereochemistry**

Wave has driven foundational advances in nucleic acid chemistry to expand platform technologies and develop next generation of RNA therapeutics

Further information can be found in recent platform publications

Silencing (RNase H and Ago2) | **Splicing** | **Editing**

Proprietary chemistry continues to translate in clinic across modalities, enabling first-in-class and best-in-class therapies



Full list of Wave publications: https://ir.wavelifesciences.com/events-publications/publications
*mHTT reductions compared to placebo

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

Program	Discovery / Preclinical	IND / CTA Enabling Studies	Clinical	Rights	Patient population (US & Europe)
RNA EDITING					
WVE-006 SERPINA1 (AATD)	RestorAATion Clinical Program			GSK exclusive global license	200K
Multiple undisclosed Correction				100% global	>20K (multiple)
Multiple undisclosed Upregulation				100% global	>3M (multiple)
RNAi					
WVE-007 Obesity and other metabolic disorders				100% global	47M
SPLICING					
WVE-N531 Exon 53 (DMD)	FORWARD-53 Trial (Phase 2)			100% global	2.3K
Other exons (DMD)				100% global	Up to 18K
ALLELE-SELECTIVE SILENCING					
WVE-003 mHTT (HD)	SELECT-HD Trial (Phase 1b/2a) - *Trial Completed*			Takeda 50:50 Option	25K Symptomatic (SNP3) 60K Pre-Symptomatic (SNP3)

Editing for correction Editing for upregulation

WAVE LIFE SCIENCES

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

WVE-006 + AIMers
RNA editing

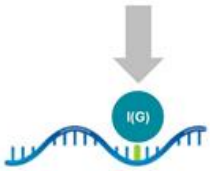
Alpha-1 antitrypsin deficiency (AATD)

WAVE LIFE SCIENCES

WVE-006: GalNAc-conjugated AIMer designed to correct mutant SERPINA1 transcript to address both liver and lung manifestations of AATD

WVE-006 for AATD

SERPINA1 Z allele mRNA encodes Z-AAT protein with E342K mutation



Edited *SERPINA1* mRNA enables wild-type M-AAT protein production

WVE-006 aims to address the large unmet need in AATD

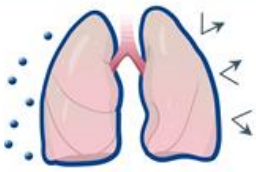
- 200,000 Pi*ZZ patients in US and Europe
- Current standard of care is weekly IV augmentation therapy
- No therapies address AATD liver disease

WVE-006 ADAR editing approach to address key goals of AATD treatment:

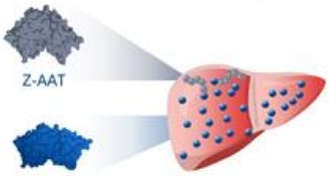
1) Restore circulating, functional wild-type M-AAT

2) Reduce Z-AAT protein aggregation in liver

3) Retain M-AAT physiological regulation



M-AAT reaches lungs to protect from proteases



RNA correction replaces mutant Z-AAT protein with wild-type M-AAT protein

M-AAT secretion into bloodstream

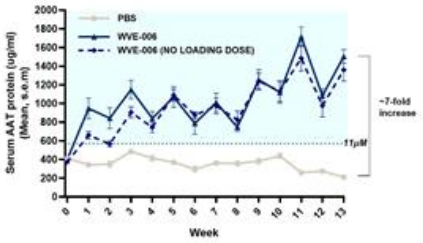
AAT: Alpha-1 antitrypsin Strnad et al., 2020 N Engl J Med 382:1443-55; Blanco et al., 2017 Int J Chron Obstruct Pulmon Dis 12:561-69; Remih et al., 2021 Curr Opin Pharmacol 59:149-56.

WVE-006 in AATD: First-in-class RNA editing clinical candidate

Potentially comprehensive approach to address both lung and liver manifestations of AATD

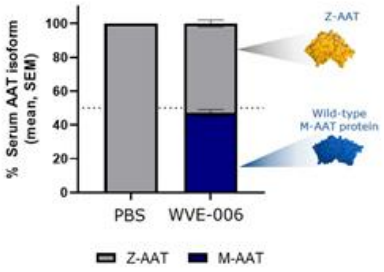
Increased AAT protein in NSG-PiZ mice

WVE-006 treatment results in serum AAT protein levels of up to 30 uM in NSG-PiZ mice



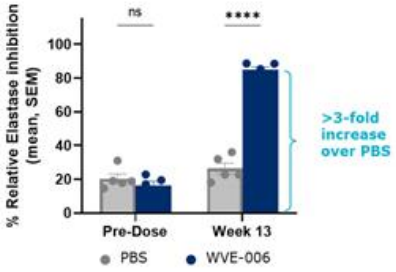
Confirmed restored wild-type M-AAT protein

Overall percentages of serum AAT protein isoforms in NSG-PiZ mice (Week 13)



Demonstrated functionality of M-AAT protein

Serum neutrophil elastase inhibition activity in NSG-PiZ mice



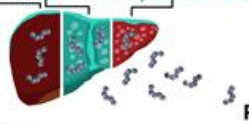
≥50% editing supports restoration of MZ phenotype

AATD: Alpha-1 antitrypsin deficiency; M-AAT protein: wild-type AAT protein; WVE-006 administered subcutaneously (10 mg/kg bi-weekly) in 7-week old NSG-PiZ mice (n=5 per group); Loading dose: 3 x 10 mg/kg at Day 0. Left: Liver biopsies collected at wk 13 (1 wk after last dose) and SERPINA1 editing quantified by Sanger sequencing; Right: Total serum AAT protein quantified by ELISA; Stats: Two-Way ANOVA with adjustment for multiple comparisons (Tukey)

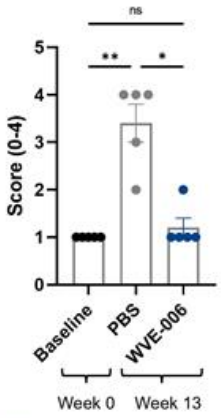
WVE-006 decreases lobular inflammation and PAS-D globule size, prevents increase in hepatocyte turnover

Correction of gain-of-function liver phenotypes

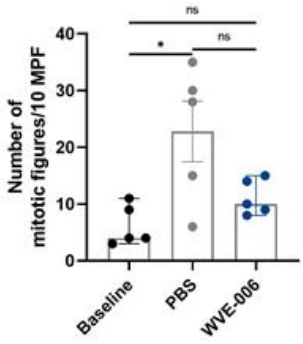
Fibrosis → Cirrhosis → Hepatocellular Carcinoma



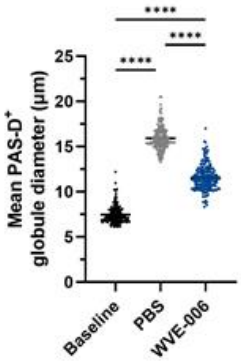
Lobular inflammation
(NSG PiZ mice, week 13)



Mitoses
(NSG PiZ mice, week 13)



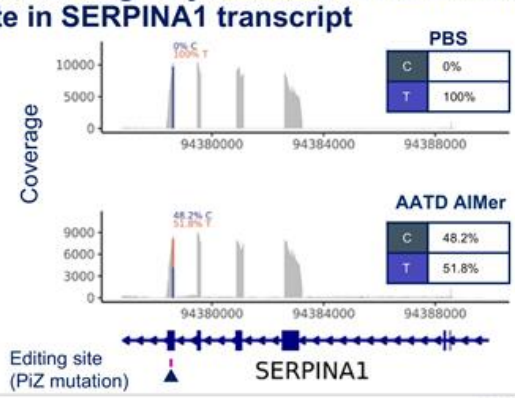
PAS-D-positive globule size
(NSG PiZ mice, week 13)



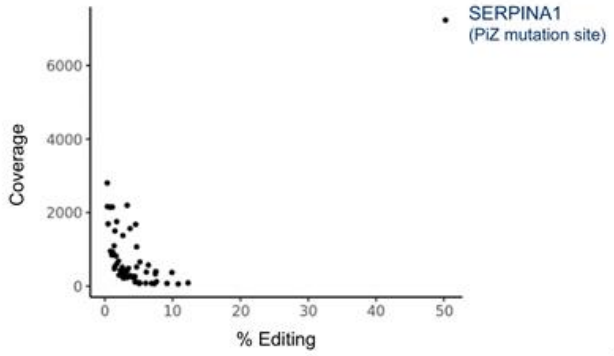
Left (Lobular inflammation) and Middle (Mitoses): Scatter plot showing inflammation grade or mitoses score. Each circle represents an individual mouse, (Mean ± SEM); Right (PAS-D Globule Size): 40 largest globules in each of 5 mice were measured. Each circle represents a single PAS-D globule, (Mean ± SEM). Baseline: week 0 (7 weeks old); Treated week 13 (20 weeks old); Stats: Kruskal-Wallis followed by Dunn's test

AIMer-directed editing is highly specific in mice

RNA editing only detected at PiZ mutation site in SERPINA1 transcript



RNA editing across transcriptome



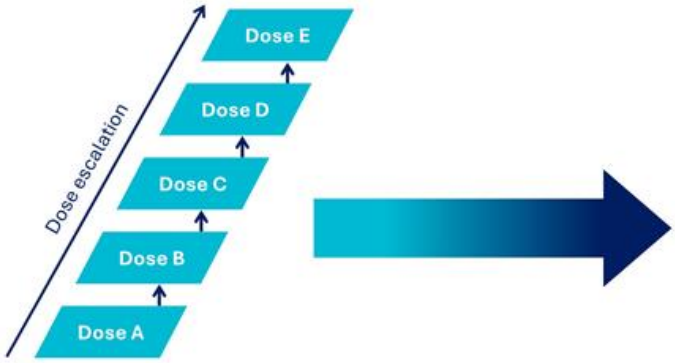
No bystander editing observed on SERPINA1 transcript

Dose 3x10 mg/kg (days 0, 2, 4) SC with AATD AIMer (SA1 – 4). Liver biopsies day 7. RNA-seq to quantify on-target SERPINA1 editing, to quantify off-target editing reads mapped to entire mouse genome; plotted circles represent sites with LOD>3 (N=4), SERPINA1 edit site is indicated

RestorAATion-2 underway, proof-of-mechanism data expected in 4Q 2024

RestorAATion-1: Healthy Volunteers → Informs dose & dose frequency → **RestorAATion-2: AATD Patients**

Single ascending dose (SAD) → Multiple-ascending dose (MAD) cohorts



Up to 7 doses

Cohort 3

Cohort 2

Cohort 1

Multiple assessments of serum AAT throughout cohort

Study key objectives

Safety and tolerability
Pharmacokinetics
Serum M-AAT levels

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

Multiple RNA editing opportunities to build high-value, wholly-owned pipeline beyond WVE-006

Potential to advance any combination of targets into preclinical development

	Hepatic (GalNAc-AIMers)				Extra-Hepatic (AIMers)	
	Target A	**Target B**	**Target X**	**Target E**	**Target F**	**Target G**
Approach	Upregulation	Upregulation	Upregulation	Correction	Upregulation	Correction
Tissue	Liver	Liver	Liver	Liver	Kidney	Lung
Therapeutic Area	Metabolic	Metabolic	Renal	Rare	Renal	Rare
Estimated Patients (US and Europe)	~90M	~3M	~170K	~17K	~85K	~5K

- The Edit-Verse is substantial and still expanding
- Advancing work for a diverse set of undisclosed targets addressing areas of high unmet need, including both rare and prevalent diseases

Strategic collaboration with GSK to develop transformative RNA medicines

Collaboration Highlights

- $170 million upfront[1]
- Additional research funding
- Potential for up to $3.3 billion in milestones[2]
- Leverage GSK's expertise in genetics and genomics

	Maximize global potential for WVE-006 for AATD	Advance up to eight GSK collaboration programs	Expand Wave's pipeline
	Up to $525 million in total milestones and **tiered royalties on net sales**	**Up to $2.8 billion** in total milestones and **tiered royalties on net sales**	Wave to advance up to **three wholly owned collaboration programs** (or more with GSK's consent)[3]
Recent Highlights	✓ **$20 million milestone** with first individual dosing RestorAATion-2 trial underway (AATD patients)	✓ **$12 million aggregate initiation payment** for GSK's selection of two programs to advance	✓ **INHBE is Wave's first wholly owned program** emerging from GSK collaboration

1. $120 million in cash and $50 million equity investment 2. Initiation, development, launch, and commercialization milestones for WVE-006 and programs progressed during initial 4-year research term (8 GSK collaboration programs), 3. GSK eligible to receive tiered royalty payments and commercial milestones from Wave

WVE-007 (INHBE program)
GalNAc-siRNA silencing

Obesity and other metabolic disorders

WAVE LIFE SCIENCES

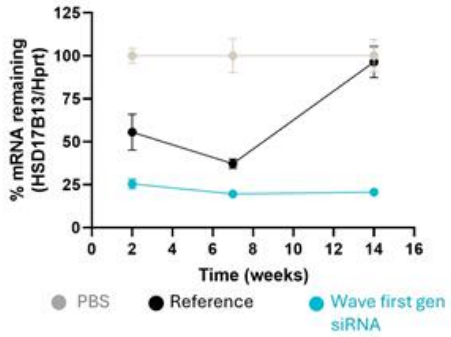
Potential for best-in-class siRNA enabled by Wave's PRISM® platform

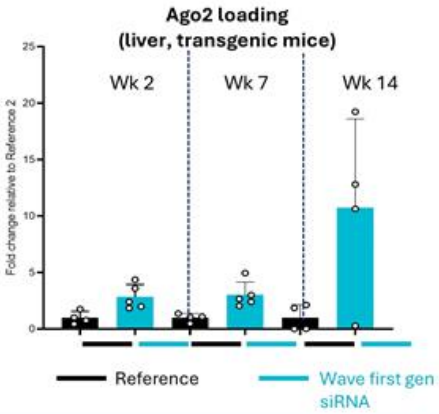
Nucleic Acids Research

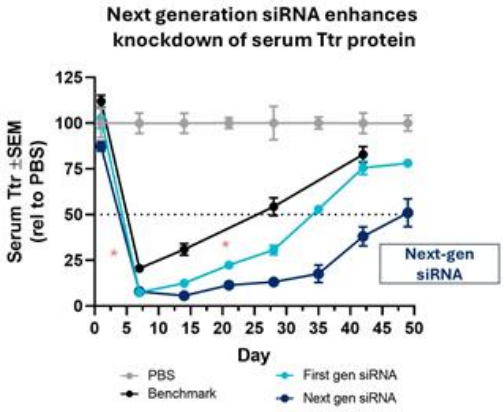
Impact of stereopure chimeric backbone chemistries on the potency and durability of gene silencing by RNA interference

- Unprecedented Ago2 loading increases potency and durability of silencing following administration of single subcutaneous dose

Next-generation siRNA results in more potent and durable silencing







siRNA silencing is one of multiple Wave modalities being advanced in strategic research collaboration with GSK

WAVE LIFE SCIENCES

Left and Middle: Mice expressing human HSD17B13 transgene treated with siRNA (3 mg/kg) or PBS, liver mRNA, guide strand concentration, Ago2 loading quantified. Stats: Two-way ANOVA with post-hoc test * P<0.05, ****P<0.0001. Liu et al., 2023 Nuc Acids Res doi: 10.1093/nar/gkad268; Right: Benchmark: Foster, DJ. et.al. Mol Ther. 2018, 26(3), 708. B6 mice administered PBS or 0.5 mg/kg of siRNA (subcutaneous). Stats: Mixed Two-way ANOVA followed by post hoc test comparing siRNA vs. Next gen siRNA per day derived from linear mixed effects model * P < 0.0001

Supported by human genetics, WVE-007 (INHBE GalNAc-siRNA) expected to drive healthy, sustainable weight loss

INHBE silencing expected to induce fat loss, while maintaining muscle mass

- Silencing INHBE gene by ≥ 50% is expected to recapitulate the healthy metabolic profile of INHBE loss of function (LoF) carriers, including:[1,2,3]

✓ Reduced waist-to-hip ratio
✓ Reduced odds ratio of type 2 diabetes and coronary artery disease by >25%
✓ Reduced serum triglycerides
✓ Elevated HDL-c

- INHBE (Inhibin βE) expressed primarily in liver and gene product (activin E) acts on its receptor in adipose tissue[4]
- Lowering of INHBE mRNA promotes fat burning (lipolysis) and decreases fat accumulation (adiposity)[5,6]

Distinct pathway as compared to GLP-1s

✓ Weight loss with no impact on muscle mass[1]
✓ Preferential reduction of visceral fat
✓ No suppression of general reward system[3]
✓ No loss of appetite
✓ GalNAc-siRNA enables infrequent dosing; 1 – 2x/year

Wave's INHBE siRNA program may address these limitations and / or work complementarily with GLP-1s

Obesity is estimated to impact 174M adults in the US and Europe

1. Sargeant, et al. 2019 Endocrinol Metab (Seoul) 34(3):247-262; 2. Prime Therapeutics Claims Analysis, July 2023; 3. Müller, et al. 2019 Molecular Metabolism 30: 72-130.

1. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 2. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8; 3. PLOS ONE 2018. https://doi.org/10.1371/journal.pone.0194798; 4. Adam, RC. et.al. Proc Natl Acad Sci USA. 2023, 120(32): e2309967120. 5. Yogosawa et al. 2013 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3526038/ 6. Zhao et al. 2023 https://pubmed.ncbi.nlm.nih.gov/36626233/

WVE-007 has Wave's next generation siRNA format and best-in-class profile with infrequent dosing

INHBE program: Data from DIO mouse model supports best-in-class profile and potential use of WVE-007 in multiple treatment settings

- ✓ Highly potent (ED50 < 1mg/kg) and durable silencing following one, low-single-digit dose, supporting every-six-month or annual dosing
- ✓ **Monotherapy:** Weight loss similar to semaglutide with no loss of muscle mass and a reduction in fat mass, with preferential effect to the visceral fat (consistent with profile of INHBE LoF carriers in human genetics)
- ✓ **Combination with GLP-1s:** When administered in combination with semaglutide, a single dose of Wave's INHBE GalNAc-siRNA doubled the weight loss observed with semaglutide alone and this effect was sustained throughout the duration of the study
- ✓ **Maintenance:** Curtailed rebound weight gain upon cessation of semaglutide

Expect to initiate clinical trial for WVE-007 in 1Q 2025

WVE-N531
Splicing

Duchenne muscular dystrophy

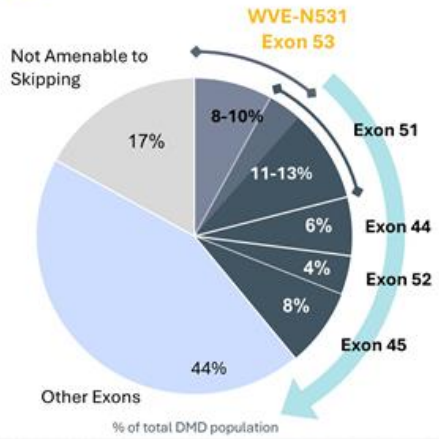
WAVE LIFE SCIENCES

Developing a best-in-class exon-skipping franchise for DMD

WVE-N531 may address high unmet need in DMD patients

- **Genetic mutation in dystrophin gene prevents the production of dystrophin protein,** a critical component of healthy muscle function
- **Impacts approx. 1 in every 5,000 newborn boys each year;** approx. 20,000 new cases annually worldwide
  - Approx. 8-10% are amenable to exon 53 skipping
- In 2023, exon skipping therapeutics for DMD achieved **~$1 billion in sales,** across exons covering approximately ~29% of the DMD population[1]
- **Dystrophin protein established by FDA as surrogate endpoint** reasonably likely to predict benefit in boys[2]

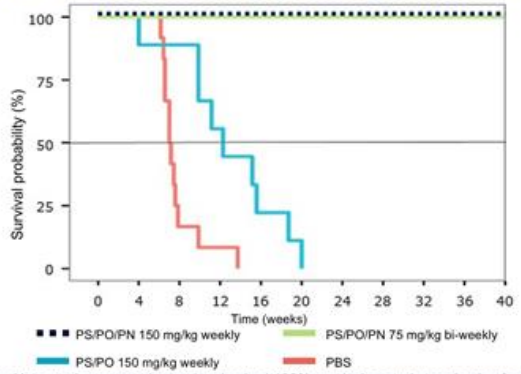
Potential to address up to 40% of DMD population[3]



1. Sarepta Therapeutics 2023 10-K and Nippon Shinyaku 2023 Annual Results; 2. Vyondys: www.fda.gov; viltepso; www.fda.gov; Exondys; www.fda.gov; Amondys: www.fda.gov
3. Aartsma-Rus, et al. 2009 Hum Mutat 30, 293.

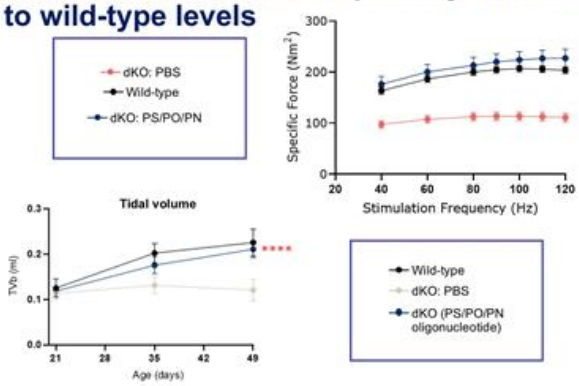
Extended survival in dKO preclinical model supports potential of Wave's PN-modified exon-skipping therapeutics for DMD

100% survival at time of study termination



Note: Untreated, age-matched mdx mice had 100% survival at study termination [not shown]

Restored muscle and respiratory function to wild-type levels

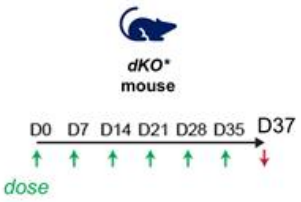


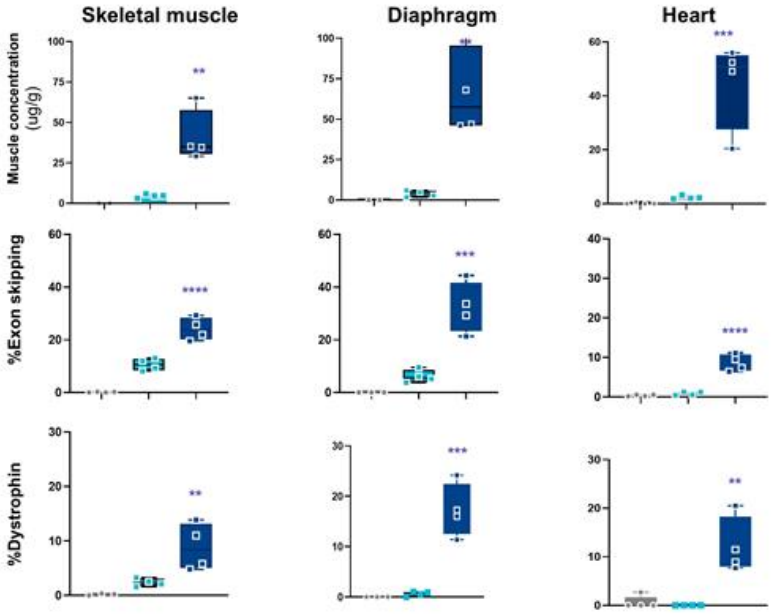
PN chemistry improved function and survival in dKO mice

Kandasamy et al., 2022; doi: 10.1093/nar/gkac018
dKO: double knock-out

Wave's PN chemistry yields excellent muscle exposure, exon skipping and dystrophin protein expression in *dKO* mouse model

- PBS
- PS/PO modified oligonucleotides for mouse exon 23
- PS/PO/PN modified oligonucleotides for mouse exon 23

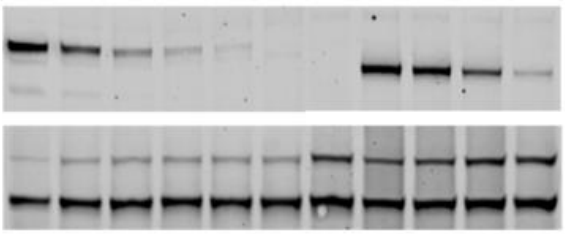




Preclinical data supported advancing WVE-N531 to clinical development

WVE-N531: Dystrophin restoration of up to 71% *in vitro* in patient-derived myoblasts

Standard Curve (% WT lysate in D45-52 lysate)						D45-52 Cells				
						Mock	WVE-N531			
						0	10	3.3	1.1	0.3
100%	50%	25%	12%	6%	0%	0%	71%	65%	37%	9.5%



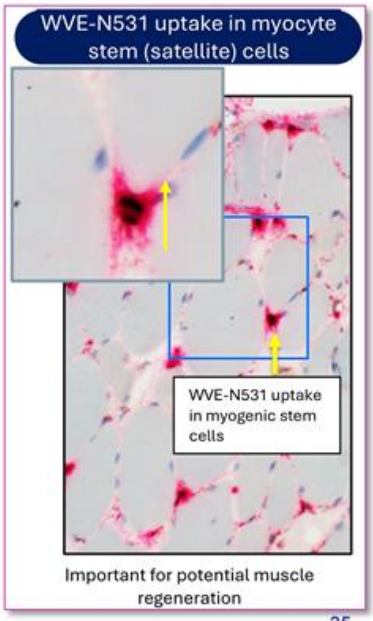
WVE-N531 reached high concentrations in heart and diaphragm in NHP

	Mean Tissue Concentration		
	Skeletal muscle	Diaphragm	Heart
15 mg/kg* IV dose	2.17 ug/g	10.8 ug/g	57.2 ug/g

*approximately equivalent to 10 mg/kg in patients based on plasma AUC values

Clinical data from WVE-N531 Part A: High exon-skipping & muscle concentrations after three doses every other week

	suvodirsen	WVE-N531
Mean muscle concentration	0.7 µg/g (~700 ng/g)	42 µg/g (~42,000 ng/g)[1]
Mean exon skipping	Not detectable	53%
Half-life in plasma	18 hours	25 days
Dose	22 weekly doses of 5 mg/kg	3 doses of 10 mg/kg every other week



1: 42 µg/g = 6.1 µM (6,100 nM), WVE-N531 data presented March 22, 2023 at Muscular Dystrophy Association Clinical and Scientific Conference; WVE-N531 biopsies collected ~2 weeks post-last dose (3 biweekly doses of 10 mg/kg); Suvodirsen biopsies collected post-last dose (weekly doses of 5 mg/kg) on week 22; Half-life as indicated by PK analysis; suvodirsen: discontinued first-generation non-PN chemistry compound; Right: Dual staining utilizing in-situ hybridization for WVE-N531 and PAX7 immunohistochemistry for stem cells. Suvodirsen N= 8; WVE-N531 N=3 boys

Advancing FORWARD-53, a potentially registrational Phase 2 clinical trial of WVE-N531 in DMD (Exon 53)

- Design of FORWARD-53: Phase 2, open-label, 10 mg/kg every other week
- Endpoints: Dystrophin (powered for >5% of normal), safety/tolerability, pharmacokinetics, digital and functional assessments (incl. NSAA and others)
- Muscle biopsies to assess dystrophin expression
- Fully enrolled (n=11) and dosing underway

FORWARD-53

Potentially registrational 24-week dystrophin expression data are expected in 3Q 2024

IV: intravenous; NSAA: North star ambulatory assessment

WVE-003
Allele-selective silencing

Huntington's Disease

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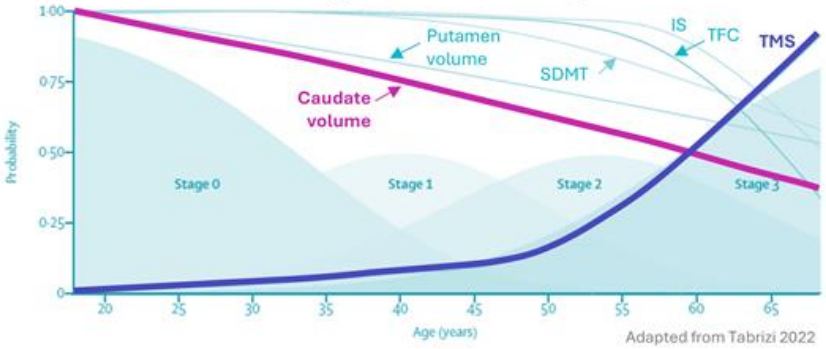
Huntington's disease is a devastating neurological disorder caused by a toxic gain of function and concurrent loss of function

- 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 in wild-type huntingtin protein (wtHTT)

HD-ISS stage probability and predicted clinical landmark changes as a function of age



Adapted from Tabrizi 2022

>200,000 patients with HD across all disease states

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

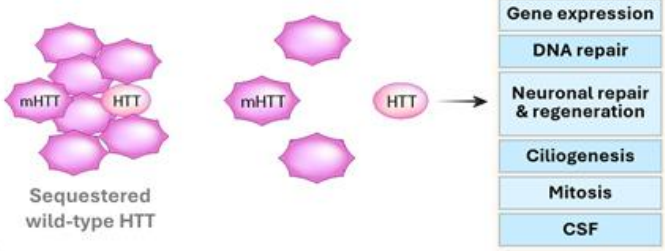
An allele-selective, wtHTT-sparing approach is uniquely suited to address HD across all stages of disease

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; IS, Independence Scale; SDMT, Symbol Digit Modalities Test; TFC, Total Functional Capacity; TMS, Total Motor Score

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

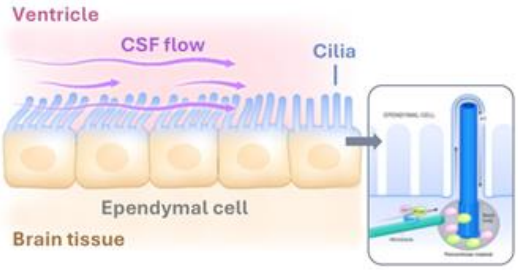
Mutant HTT has a detrimental effect on wild-type HTT function

- 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



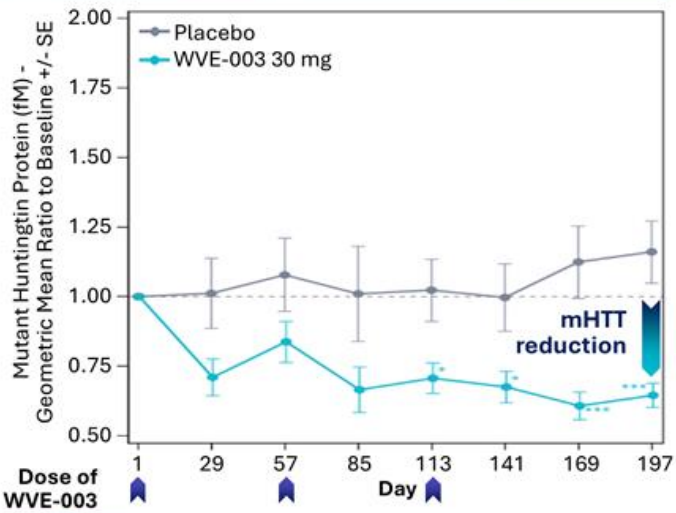
Only an allele-selective approach can ameliorate both loss-of-function and gain-of-function disruptions driven by mHTT

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

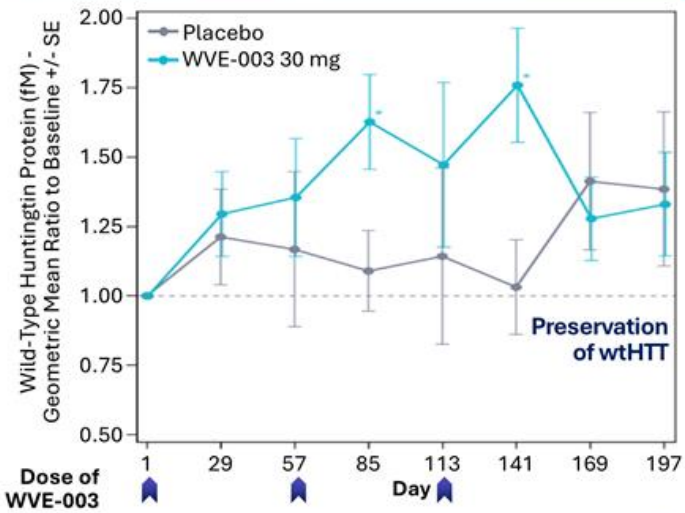
Allele-selective lowering of mutant HTT protein of up to 46% with three doses of WVE-003 and preservation of wild-type HTT

Durability of mHTT reductions supports potential for quarterly dosing intervals

Mutant HTT protein levels



Wild-type HTT protein levels



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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

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

Allele-Selective mHTT KD with wtHTT Preservation

- mHTT reduction of up to 46% vs. placebo
- wtHTT preserved/increased throughout study

Slowing of Caudate Atrophy

- WVE-003 trended towards less caudate atrophy vs. placebo (4.68% vs. 5.10%, not significant)

Functional Benefit

- Caudate atrophy is an imaging biomarker expected to predict clinical outcomes, including clinically meaningful worsening of Total Motor Score (TMS)

Greater allele-selective mHTT reduction correlated with the slowing of caudate atrophy at 24 weeks (R = -0.50, p=0.047)

Liu et al., 2023 Brain Comm

Preservation of caudate volume offers an efficient pathway for potential accelerated approval for HD

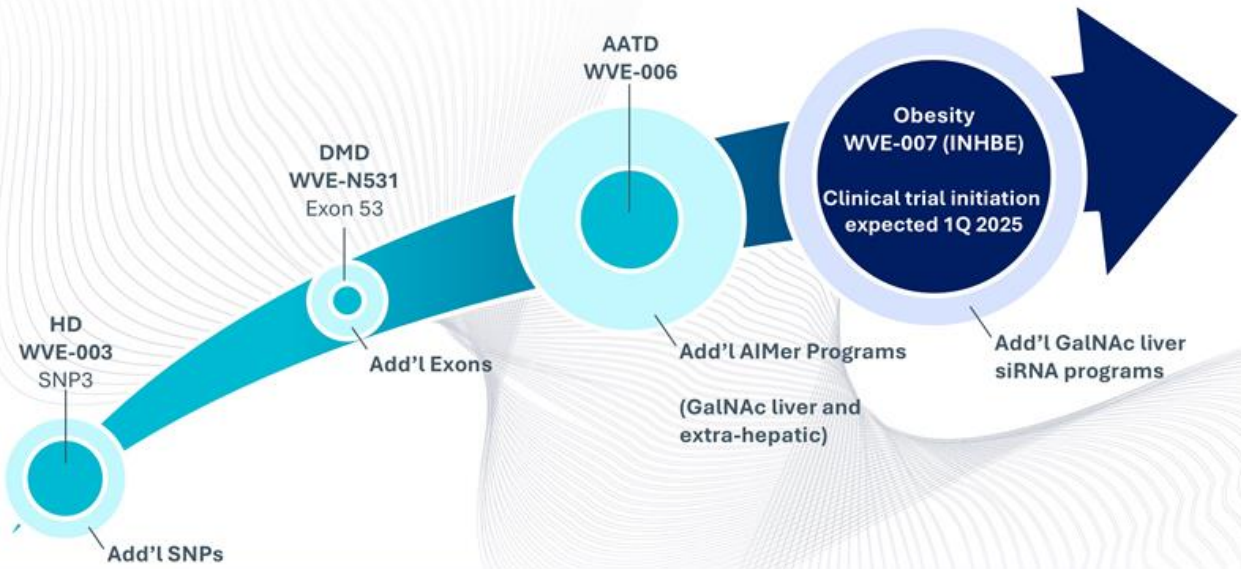
Draft study design: Registrational study powered to show impact on caudate atrophy	• Randomized, placebo controlled clinical study Adults with SNP3 and HD Stage 1-2 • N = ~150 • 12-18 months duration

Expect feedback from regulators on path to accelerated approval by year-end 2024

vMRI: volumetric MRI

Anticipated upcoming milestones

Wave is poised for significant and sustained growth



Wave's platform is translating in the clinic, with DMD and AATD data updates expected in 2024 and advancement of WVE-007 to clinic in 1Q 2025 (INHBE)

Note: Bubble size illustrative of size of total addressable US market (assuming 100% share of addressable patients)

Anticipated milestones in 2024 and beyond

WVE-006 (AATD) *Most advanced clinical RNA editing candidate & potential best-in-class approach for AATD*	**4Q 2024:** Deliver proof-of-mechanism data from RestorAATion clinical program
WVE-007 (Obesity) *Driven by protective LoF variants in human genetics, potential next-gen therapeutic for obesity*	**1Q 2025:** Initiate clinical trial for WVE-007
WVE-N531 (DMD) *Potential best-in-class approach with highest exon skipping reported*	**3Q 2024:** Deliver potentially registrational 24-week dystrophin expression data from FORWARD-53
WVE-003 (HD) *First-in-class allele-selective mHTT lowering, wtHTT-sparing approach*	**By year-end 2024:** Expect to receive decision from Takeda on option right and feedback from regulators on a clinical development path

Potential for GSK and Takeda collaboration milestones in 2024
R&D Day expected in the Fall 2024

AATD: Alpha-1 antitrypsin deficiency; DMD: Duchenne muscular dystrophy; HD: Huntington's disease; mHTT: Mutant huntingtin; wtHTT: Wild-type huntingtin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