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): March 6, 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 March 6, 2024, Wave Life Sciences Ltd. (the "Company") announced its financial results for the quarter and year ended December 31, 2023. 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 March 6, 2024, the Company updated its corporate presentation, which is available on the "For Investors & Media" 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 March 6, 2024
99.2	Corporate Presentation of Wave Life Sciences Ltd. dated March 6, 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: March 6, 2024

Wave Life Sciences Reports Fourth Quarter and Full Year 2023 Financial Results and Provides Business Update

INHBE lead clinical candidate selected; potential best-in-class treatment for obesity with potent and durable silencing, weight loss with no loss of muscle mass, reduction of visceral fat, and every-six-month or annual subcutaneous dosing; clinical trial initiation expected 1Q 2025

Dose escalation ongoing in RestorAATion-1 clinical trial of WVE-006, industry's first-ever RNA editing candidate in the clinic; GalNAc pharmacology translating as expected and proof-of-mechanism data from patients with AATD in RestorAATion-2 on track for 2024

Dystrophin data from potentially registrational FORWARD-53 trial of WVE-N531 in DMD on track for 3Q 2024; industry-leading exon skipping levels, muscle tissue concentrations, and myogenic stem cell distribution achieved in Part A clinical trial

WVE-003 multi-dose data in HD with extended follow-up on track for 2Q 2024; first-in-class program designed to lower mutant HTT while sparing wild-type HTT

Cash and cash equivalents of $200 million as of December 31, 2023; additional $34 million received in 1Q 2024 in a milestone payment from GSK and net proceeds from full exercise of greenshoe option, with runway expected into 4Q 2025; additional anticipated payments under existing collaborations in 2024 and beyond

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

CAMBRIDGE, Mass., March 6, 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 fourth quarter and full year ended December 31, 2023, and provided a business update.

"Following a year of execution and tremendous progress, we entered 2024 well-capitalized and uniquely positioned to deliver multiple high-impact clinical data readouts across three different modalities and unlock the broad potential of our pipeline in both rare and prevalent diseases," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We are rapidly accelerating the development of our next generation GalNAc-siRNA INHBE program in obesity and are encouraged by the emerging preclinical data, which supports a potential best-in-class profile for this program. These data demonstrate greater knockdown, potency, and durability following a low, single dose, compared to our first generation data, and importantly, demonstrate substantial weight loss with decreases in fat mass and no loss of muscle mass."

Dr. Bolno continued, "In parallel with our efforts to advance our INHBE program, we are continuing to progress our clinical trials. We remain at the forefront of innovation in RNA editing and expect to deliver proof-of-mechanism data for WVE-006 in AATD in 2024. These data would unlock our rapidly advancing pipeline of wholly owned editing candidates. Beyond editing, we remain on track to deliver multidose data for our novel, allele-selective HD program in the second quarter and potentially registrational data from our FORWARD-53 trial in DMD in the third quarter. The coming months have the potential to be truly transformative for Wave."

Recent Business Highlights

AATD and AIMer pipeline (RNA editing)

- **Dose escalation in RestorAATion-1 clinical trial ongoing; clinical program investigating WVE-006 as a first- and best-in-class treatment for alpha-1 antitrypsin deficiency (AATD).**
  - WVE-006 is a GalNAc-conjugated, subcutaneously delivered, RNA editing oligonucleotide that is uniquely designed to address AATD-related lung disease, liver disease, or both.
  - The RestorAATion clinical program is evaluating WVE-006 for AATD and includes healthy volunteers (RestorAATion-1), as well as patients who have the homozygous Pi*ZZ mutation (RestorAATion-2). It is designed to provide an efficient path to proof-of-mechanism as measured by restoration of wild-type alpha-1 antitrypsin (M-AAT) protein in serum.
  - In the fourth quarter of 2023, Wave initiated dosing in RestorAATion-1, which resulted in a $20 million milestone payment from GSK. Dose escalation is ongoing and WVE-006's pharmacology in healthy volunteers is translating as expected.
  - Beyond WVE-006, Wave is advancing a pipeline of wholly owned RNA editing therapeutics across a range of high-impact GalNAc-hepatic and extra-hepatic targets. Utilizing its proprietary "edit-verse," which is powered by genetic datasets and deep learning models, Wave has identified several new RNA editing targets that leverage easily accessible biomarkers, offer efficient paths to proof-of-concept in humans, and represent meaningful commercial opportunities. Wave plans to share new preclinical data for its advancing RNA editing programs in 2024.
  - **Expected upcoming milestone:** Wave expects to deliver proof-of-mechanism data from RestorAATion-2 in patients with AATD in 2024.

Obesity (siRNA)

- **Selected lead clinical candidate for INHBE program with a potentially best-in-class profile for obesity and accelerated clinical development timeline.**
  - Today, Wave announced the selection of its INHBE lead clinical candidate, ahead of prior expectations, and now plans to submit a clinical trial application for its INHBE program as early as year-end 2024.
  - Wave's INHBE clinical candidate is a GalNAc-small interfering RNA (siRNA) that utilizes Wave's next generation siRNA format and is designed to silence the INHBE (Inhibin ßE) gene through RNA knockdown with a goal of inducing lipolysis (fat-burning) while preserving muscle mass to restore and maintain a healthy metabolic profile.
  - INHBE loss-of-function (LoF) heterozygous human carriers have a favorable cardiometabolic profile, including reduced abdominal obesity and reduced odds of type 2 diabetes and coronary artery disease. Silencing INHBE is expected to recapitulate the cardiometabolic profile of these LoF carriers and may also address the limitations of GLP-1s as a monotherapy or be used as an adjunct therapy with GLP-1s.

- Key data highlights from preclinical mouse models include:
    - Highly potent silencing (ED50 < 1mg/kg)
    - Durable silencing following one, low-single-digit dose supporting every-six-month or annual subcutaneous dosing
    - Weight loss with no loss of muscle mass
    - Reduction in fat mass with preferential effects on visceral fat, consistent with the profile of INHBE LoF carriers in human genetics
- **Expected upcoming milestone:** Wave expects to initiate a clinical trial for its INHBE candidate in the first quarter of 2025.

DMD (exon skipping)

- **Advancing FORWARD-53 clinical trial; multiple presentations at MDA Clinical & Scientific Conference highlight differentiated profile including industry-leading exon-skipping, muscle tissue concentrations and myogenic stem cell distribution.**
    - Wave's WVE-N531 program for boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping is designed to induce production of endogenous, functional dystrophin protein.
    - This week, at the 2024 MDA Clinical & Scientific Conference, Wave presented multiple posters highlighting WVE-N531. These posters featured data from Part A of Wave's WVE-N531 trial, demonstrating industry-leading exon skipping levels of 53% and muscle tissue concentrations of 42 µg/g (42,000 ng/g), as well as stem cell distribution in all study participants.
    - WVE-N531 is currently being evaluated in the ongoing FORWARD-53 clinical trial of 11 boys with DMD, which is powered to evaluate functional, endogenous dystrophin expression following 24 and 48 weeks of 10 mg/kg dosing administered every-other-week. The primary endpoint is dystrophin protein levels, and the trial will also evaluate pharmacokinetics, digital and functional endpoints, and safety and tolerability.
    - Pending positive results from the FORWARD-53 trial, the company is planning to advance a broader DMD pipeline with PN-modified oligonucleotides for skipping other exons, with the goal of providing new treatment options for a larger population of boys with DMD.
    - **Expected upcoming milestone:** Wave expects to deliver data, including dystrophin protein expression from muscle biopsies at 24 weeks, in the third quarter of 2024.

HD (antisense silencing)

- **WVE-003 and wild-type HTT sparing highlighted at annual CHDI Conference.**
    - WVE-003 is a first-in-class investigational allele-selective Huntington's disease (HD) therapeutic designed to reduce mutant huntingtin (mHTT) protein while also sparing healthy wild-type huntingtin (wtHTT) protein. Due to the significance of wtHTT function for the health of the central nervous system and the potential for mHTT to disrupt wtHTT function, selectively lowering mHTT while preserving wtHTT protein expression and function may offer advantages over nonselective HTT-lowering approaches for the treatment of HD.
    - WVE-003 has demonstrated single-dose reductions in mean mHTT in cerebrospinal fluid of 35% compared to placebo, with preservation of wtHTT, as previously shared in September 2022.
    - The ongoing multi-dose portion of the SELECT-HD clinical trial is evaluating a cohort of 24 patients with HD receiving 30 mg doses of WVE-003 administered every eight weeks.
    - Data from the ongoing SELECT-HD clinical trial will form the basis for decision making for Wave's advancement of this program, including supporting an opt-in package for Takeda.
    - **Expected milestone:** Wave expects to report data from the 30 mg multi-dose cohort with extended follow-up, along with all single-dose data, in the second quarter of 2024.

Financial Highlights

- Cash and cash equivalents were $200.4 million as of December 31, 2023, compared to $88.5 million as of December 31, 2022. The increase in cash year-over-year is primarily due to the $170.0 million of cash received from the GSK Collaboration and the $93.6 million in net proceeds from the December 2023 Offering, partially offset by the net loss for the year. Subsequent to December 31, 2023, Wave received $20 million in a milestone payment from GSK and $14.0 million in net proceeds from the full exercise of the greenshoe option related to the December 2023 financing.
- 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 under the company's GSK and Takeda collaborations are not included in its cash runway.
- Revenue was $29.1 million for the fourth quarter of 2023 as compared to $1.2 million in the prior year quarter. Revenue was $113.3 million in 2023 as compared to $3.6 million in 2022. The increase in revenue was due to revenue earned from the company's collaborations with both GSK and Takeda.
- Research and development expenses were $34.1 million in the fourth quarter of 2023 as compared to $31.1 million in the same period in 2022. Research and development expenses for the full year were $130.0 million in 2023, as compared to $115.9 million in 2022.
- General and administrative expenses were $13.7 million in the fourth quarter of both 2023 and 2022. General and administrative expenses for the full year were $51.3 million in 2023, as compared to $50.5 million in 2022.
- Net loss was $16.3 million for the fourth quarter of 2023 as compared to $43.7 million in the prior year quarter. Net loss for the full year was $57.5 million for 2023 as compared to $161.8 million in 2022. Net loss significantly improved over the prior year due to the substantial revenue earned from collaboration partners in 2023.

Investor Conference Call and Webcast Wave will host an investor conference call today at 8:30 a.m. ET to review the fourth quarter and full year 2023 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 announcement of such events; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; future preclinical activities and programs; regulatory submissions; 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; 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 our GalNAc-conjugated siRNA program targeting INHBE; the potential benefits that our "edit-verse" may provide us to identify 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; 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, 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)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 200,351	$ 88,497
Accounts receivable	21,086	—
Prepaid expenses	9,912	7,932
Other current assets	4,024	2,108
Total current assets	235,373	98,537
Long-term assets:		
Property and equipment, net of accumulated depreciation of $42,709 and $37,846 as of December 31, 2023 and 2022, respectively	13,084	17,284
Operating lease right-of-use assets	22,637	26,843
Restricted cash	3,699	3,660
Other assets	156	62
Total long-term assets	39,576	47,849
Total assets	$ 274,949	$ 146,386
Liabilities, Series A preferred shares and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 12,839	$ 16,915
Accrued expenses and other current liabilities	16,828	17,552
Current portion of deferred revenue	150,059	31,558
Current portion of operating lease liability	6,714	5,496
Total current liabilities	186,440	71,521
Long-term liabilities:		
Deferred revenue, net of current portion	15,601	79,774
Operating lease liability, net of current portion	25,404	32,118
Other liabilities	—	190
Total long-term liabilities	41,005	112,082
Total liabilities	$ 227,445	$ 183,603
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2023 and 2022	$ 7,874	$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 119,162,234 and 86,924,643 shares issued and outstanding at December 31, 2023 and 2022, respectively	$ 935,367	$ 802,833
Additional paid-in capital	129,237	119,442
Accumulated other comprehensive loss	(124)	(29)
Accumulated deficit	(1,024,850)	(967,337)
Total shareholders' equity (deficit)	39,630	(45,091)
Total liabilities, Series A preferred shares and shareholders' equity (deficit)	$ 274,949	$ 146,386

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

(In thousands, except share and per share amounts)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2023	2022	2023	2022
Revenue	$ 29,056	$ 1,239	$ 113,305	$ 3,649
Operating expenses:				
Research and development	34,074	31,078	130,009	115,856
General and administrative	13,664	13,724	51,292	50,513
Total operating expenses	47,738	44,802	181,301	166,369
Loss from operations	(18,682)	(43,563)	(67,996)	(162,720)
Other income, net:				
Dividend income and interest income, net	1,844	825	7,928	1,571
Other income (expense), net	582	(290)	1,878	7
Total other income, net	2,426	535	9,806	1,578
Loss before income taxes	(16,256)	(43,028)	(58,190)	(161,142)
Income tax benefit (provision)	—	(681)	677	(681)
Net loss	$ (16,256)	$ (43,709)	$ (57,513)	$ (161,823)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.15)	$ (0.47)	$ (0.54)	$ (2.05)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	109,627,549	93,993,638	106,097,268	78,855,810
Other comprehensive loss:				
Net loss	$ (16,256)	$ (43,709)	$ (57,513)	$ (161,823)
Foreign currency translation	58	94	(95)	(210)
Comprehensive loss	$ (16,198)	$ (43,615)	$ (57,608)	$ (162,033)

Investor Contact:

Kate Rausch
+1 617-949-4827
krausch@wavelifesci.com

Media Contact:

Alicia Suter
+1 617-949-4817
asuter@wavelifesci.com

Exhibit 99.2

Wave Life Sciences

Corporate Presentation

March 6, 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

AATD (RNA editing), DMD (splicing), and HD (antisense) clinical programs advancing

INHBE program for obesity (siRNA) designed for fat loss, muscle sparing, improved metabolic profile

Multi-modal drug discovery and development platform; therapeutic candidates that optimally address disease biology

Leader in RNA editing with best-in-class oligonucleotide chemistry

In-house GMP manufacturing; Strong and broad IP portfolio

Strategic collaborations to expand and advance pipeline

Well-capitalized with cash runway into 4Q 2025*

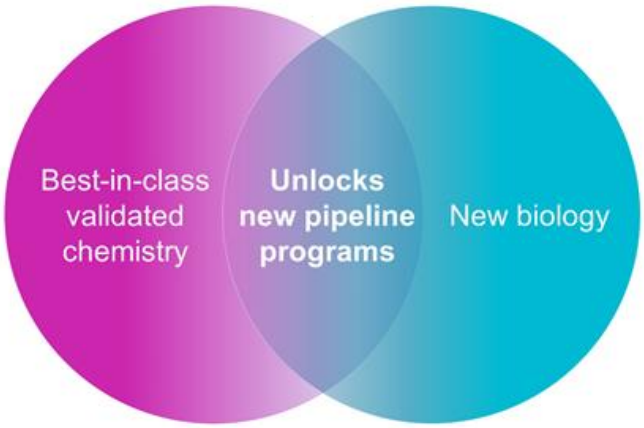
Anticipated Upcoming Milestones

- Proof-of-mechanism data from RestorAATion clinical program of WVE-006 for AATD in 2024
- Initiate clinical trial of INHBE candidate for obesity in 1Q 2025
- Data from FORWARD-53 clinical trial of WVE-N531 for DMD in 3Q 2024
- Data from SELECT-HD clinical trial of WVE-003 for HD in 2Q 2024

WAVE LIFE SCIENCES

*Cash runway does not include potential future milestones or opt-in payments under GSK and Takeda collaborations

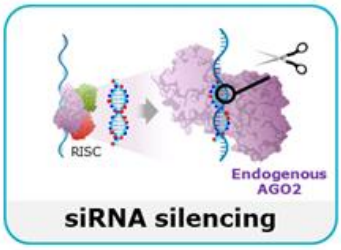
Combining best-in-class chemistry with novel biology and genetic insights: Opportunities for new high-impact medicines



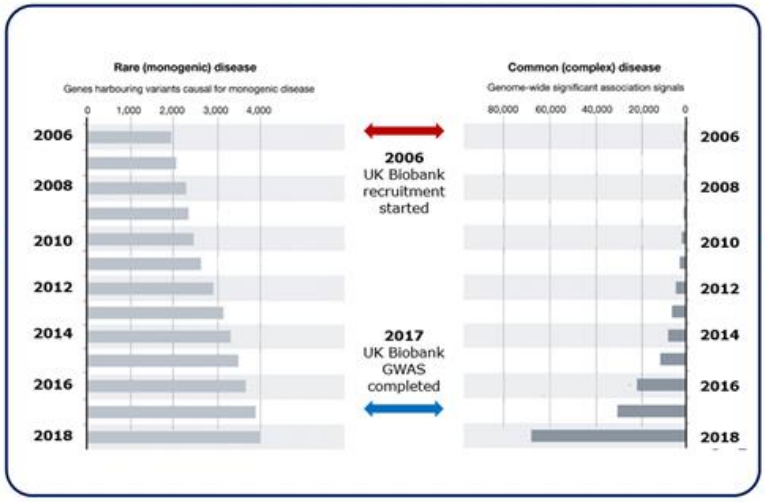
- Accessing new endogenous enzymes for novel modalities (RNA editing)
- Opening up new targets, including prevalent diseases

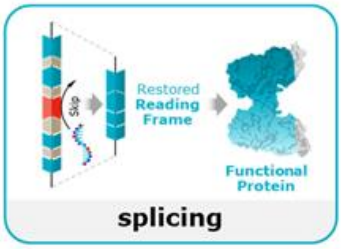
Wave's versatile RNA medicines platform ideal for capitalizing on new genetic insights in rare and common diseases

editing

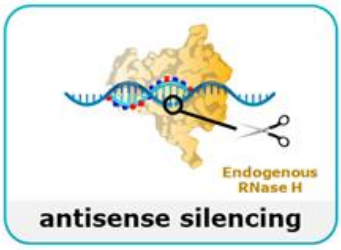


siRNA silencing





splicing



antisense silencing

Accessing UK Biobank and building proprietary machine learning models to generate unique genetic insights

Claussnitzer, et al. Nature (2020) 577, 179; King et al. PLoS Genet (2019) 15, e1008489

Robust 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)
SILENCING: siRNA					
INHBE lead clinical candidate (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
SILENCING: ANTISENSE					
WVE-003 mHTT (HD)			SELECT-HD Trial (Phase 1b/2a)	Takeda 50:50 Option	25K Manifest (SNP3) 60K Pre-Manifest (SNP3)

Editing for correction Editing for upregulation

WAVE LIFE SCIENCES

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

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 $505 million in additional 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** achieved with first individual dosing in 4Q 2023	✓ Advancing work on **multiple targets spanning multiple modalities** beyond RNA editing, including siRNA	✓ **INHBE is Wave's first wholly owned program** emerging from GSK collaboration

1. $120 million in cash and $50 million equity investment received in January 2023, 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-006 (RNA editing)

AATD

WVE-006: 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

WVE-006
(GalNAc-conjugated AIMer)

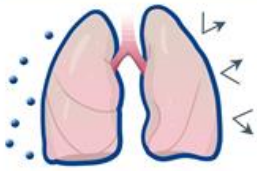
Edited *SERPINA1* mRNA enables wild-type M-AAT protein production

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

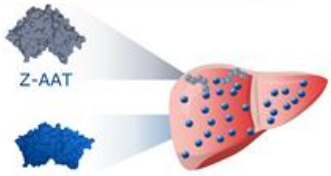
1) Restore circulating, functional wild-type M-AAT

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

200,000 Pi*ZZ patients in US and Europe

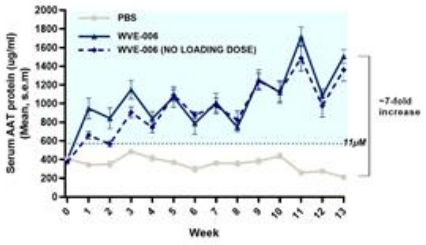
AAT: Alpha-1 antitrypsin Strnad et al., 2020 N Engl J Med 382:1443-55; Blanco et al., 2017 Int J Chron Obstruct Pulmon Dis 12:561-69; Remih et al., 2021 Curr Opin Pharmacol 59:149-56.

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

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

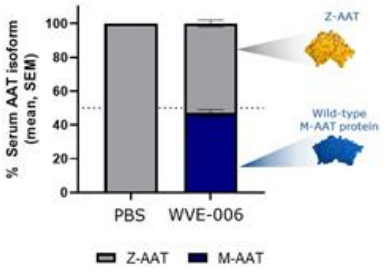
Increased AAT protein in NSG-PiZ mice

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



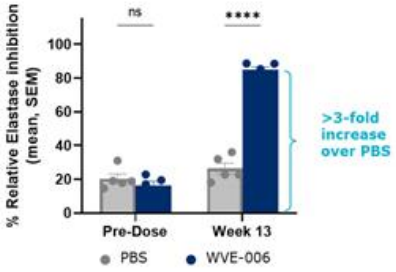
Confirmed restored wild-type M-AAT protein

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



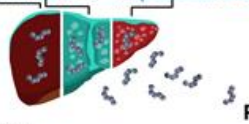
≥50% editing supports restoration of MZ phenotype

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)

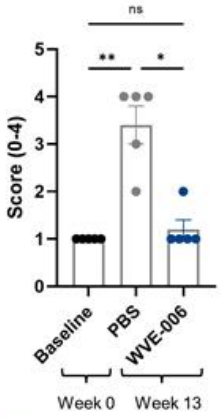
WVE-006 decreases lobular inflammation and PAS-D globule size, prevents increase in hepatocyte turnover

Correction of gain-of-function liver phenotypes

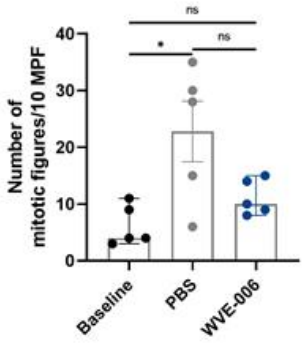
Fibrosis → Cirrhosis → Hepatocellular Carcinoma



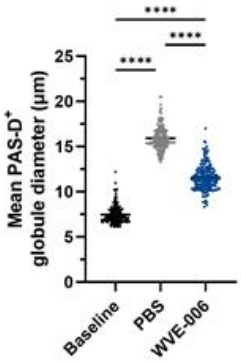
Lobular inflammation
(NSG PiZ mice, week 13)



Mitoses
(NSG PiZ mice, week 13)



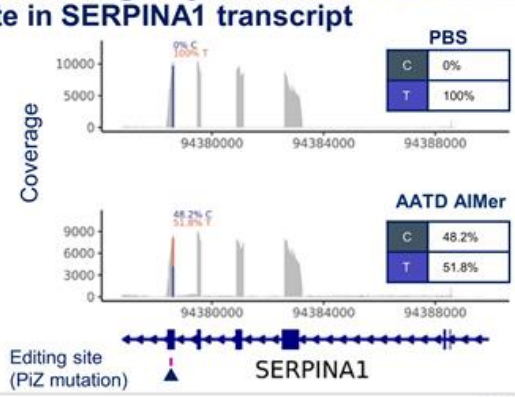
PAS-D-positive globule size
(NSG PiZ mice, week 13)



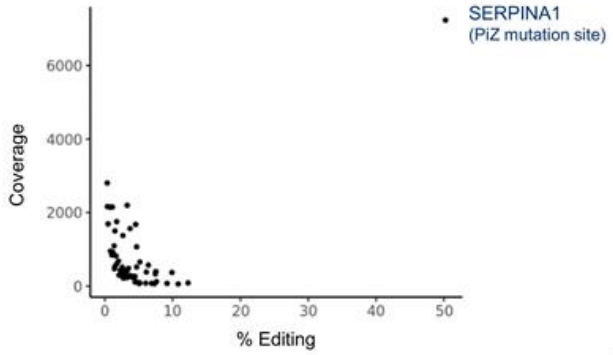
Left (Lobular inflammation) and Middle (Mitoses): Scatter plot showing inflammation grade or mitoses score. Each circle represents an individual mouse, (Mean ± SEM); Right (PAS-D Globule Size): 40 largest globules in each of 5 mice were measured. Each circle represents a single PAS-D globule, (Mean ± 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



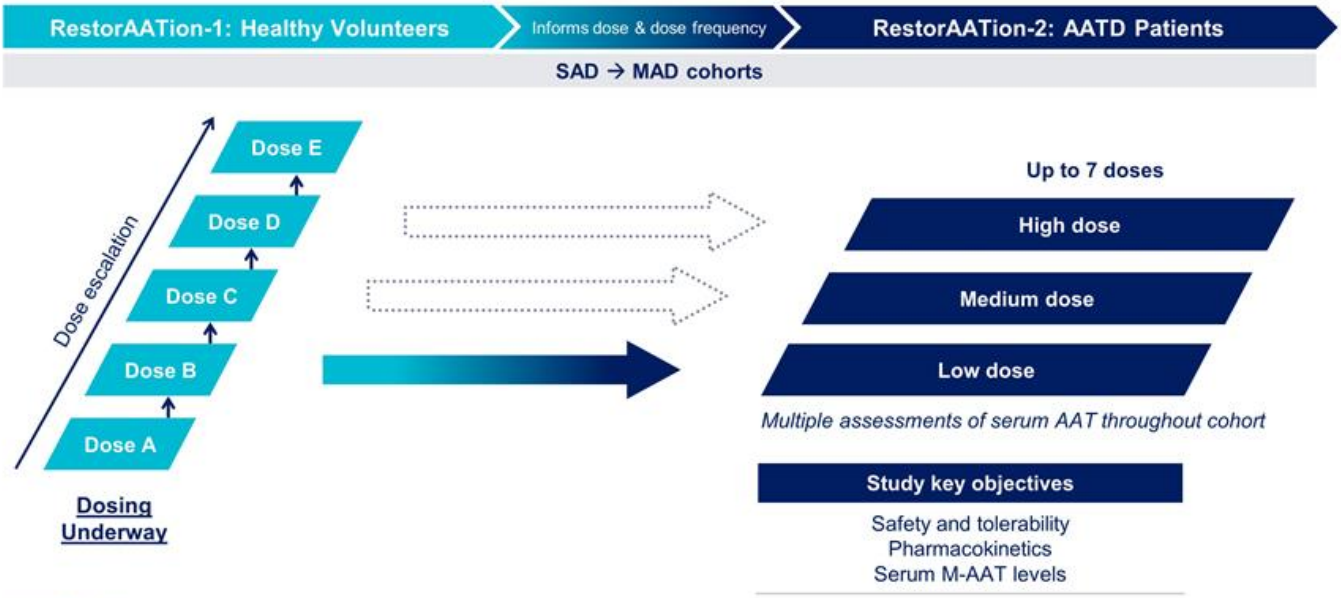
RNA editing across transcriptome



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

Proof-of-mechanism data from RestorAATion-2 expected in 2024



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

AIMers

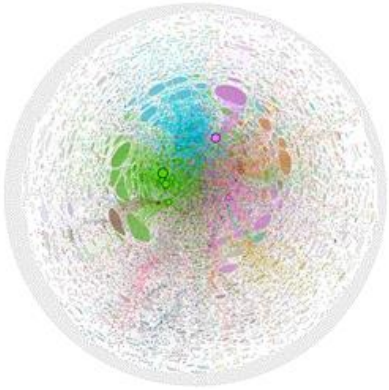
RNA editing capability

WAVE LIFE SCIENCES

The AIMer-targetable 'Edit-Verse' is substantial

- **The Edit-verse is the editable gene-disease universe, including upregulation**
- **>13,000 genes** with a high-probability[1] of being amenable to transcriptional regulation with A-to-G editing
- Model development ongoing to expand access to **more protein-coding genes** and expand the Edit-verse
- AIMers are expected to be able to target ~50% of the transcriptome

Gene-Disease Network



WAVE LIFE SCIENCES

[1](score >95th p-tile)

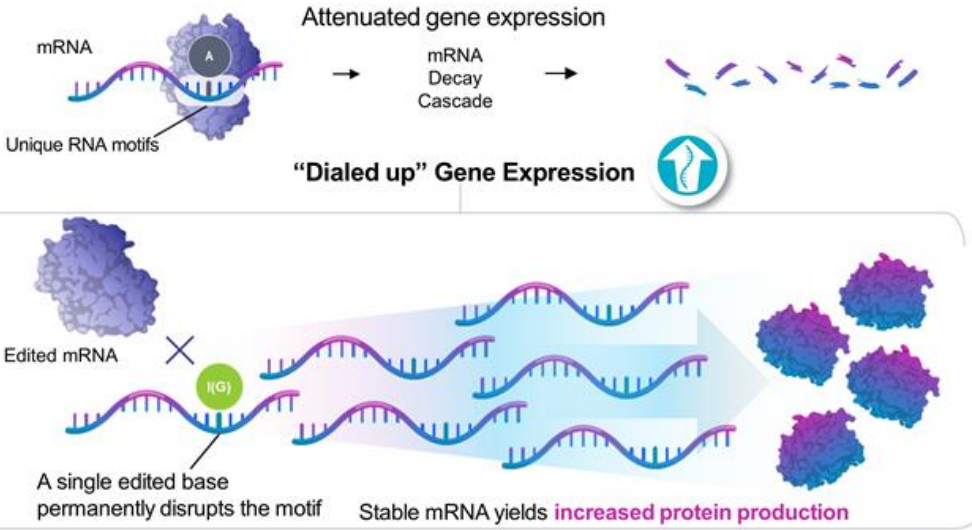
Innovating on applications of ADAR beyond restoring protein function

Restore or correct protein function

- Correct G-to-A driver mutations with AIMers

WVE-006
(GalNAc-AIMer)
AATD

Upregulate expression to increase endogenous protein activity



Multiple RNA editing opportunities to build high-value 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

INHBE program (siRNA silencing)

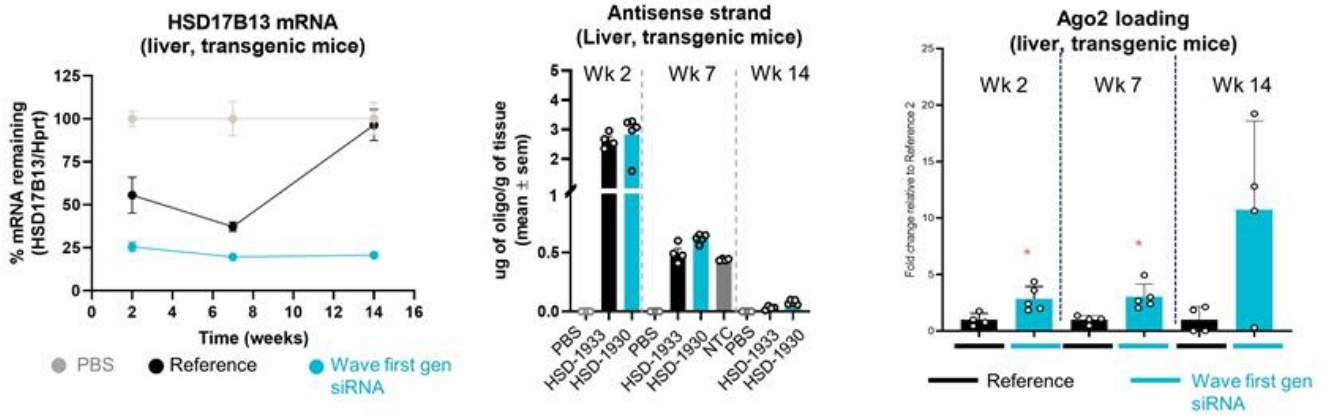
Obesity and other metabolic disorders

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



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

Left, Middle, and right: 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;

Driven by clinical genetics, Wave's first RNAi program addresses high unmet need in obesity

INHBE program (GalNAc-siRNA) is Wave's first wholly owned program to emerge from GSK collaboration

GLP-1 receptor agonists have several reported limitations

- × Lead to weight loss at the expense of muscle mass[1]
- × Associated with poor tolerability profile[4] with 68% drop-off after 1 year[3]
- × Discontinuation of therapy leads to rapid weight regain
- × Suppress general reward system[4]

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

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

- siRNA to silence INHBE gene is expected to recapitulate the healthy metabolic profile of INHBE loss of function (LoF) heterozygous human 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 expressed primarily in liver and gene product (activin E) acts on its receptor in adipose tissue[4]
- Lowering of INHBE mRNA or blocking of its receptor promotes fat burning (lipolysis) and decreases fat accumulation (adiposity)[5,6]

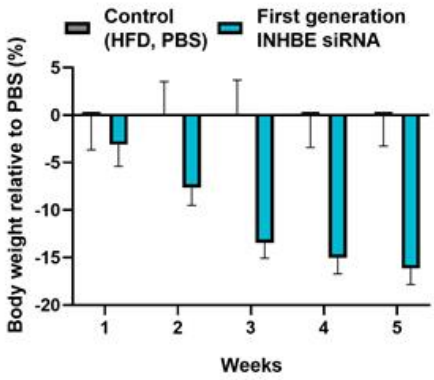
≥50% reduction of INHBE in patients expected to restore and maintain a healthy metabolic profile

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.

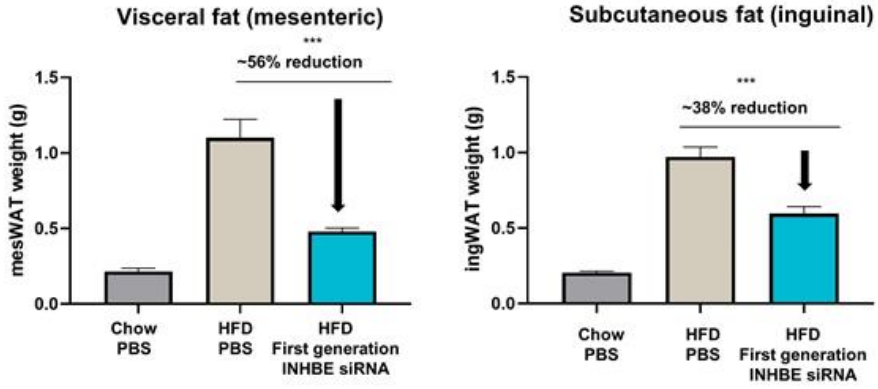
1. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 2. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8; 3. PLOS ONE 2018. https://doi.org/10.1371/journal.pone.0194798; 4. Adam, RC. et.al. Proc Natl Acad Sci USA. 2023, 120(32): e2309967120. 5. Yogosawa et al. 2013 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3526038/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

First generation INHBE GalNAc-siRNA led to lower body weight and significant decrease in visceral fat in DIO mouse model

Lower body weight as compared to control



Reduction in fat mass across multiple types of white adipose tissue, with preferential effect on visceral fat reduction

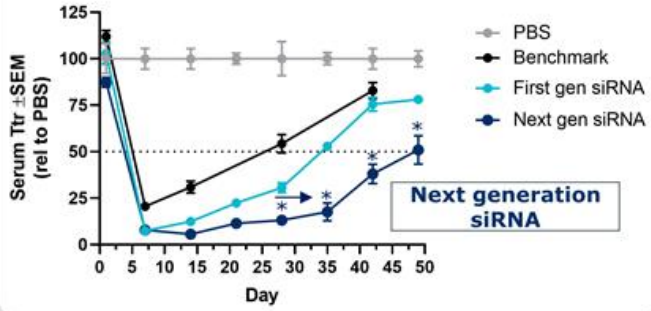


Results of *in vivo* preclinical study are consistent with UK Biobank human data on loss-of-function carriers

Right: Reduction in fat mass at Week 5

INHBE lead clinical candidate has Wave's next generation siRNA format and best-in-class profile

Next generation siRNA results in more potent and durable target knockdown



INHBE program: Data from DIO mouse model supports best-in-class profile

- ✓ Highly potent silencing (ED50 < 1mg/kg)
- ✓ Durable silencing following one, low-single-digit dose, supporting every-six-month or annual dosing
- ✓ Weight loss with no loss of muscle mass
- ✓ Reduction in fat mass, with preferential effect to the visceral fat

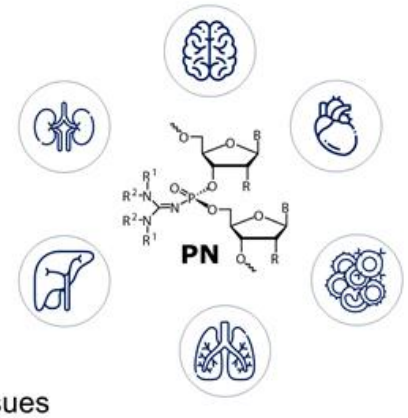
Expect to initiate clinical trial for INHBE candidate in 1Q 2025

Foster, DJ. et.al. Mol Ther. 2018, 26(3), 708. B6 mice administered PBS or 0.5 mg/kg of siRNA (subcutaneous). Benchmark: 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

Wave's platform chemistry enables siRNA extra-hepatic delivery

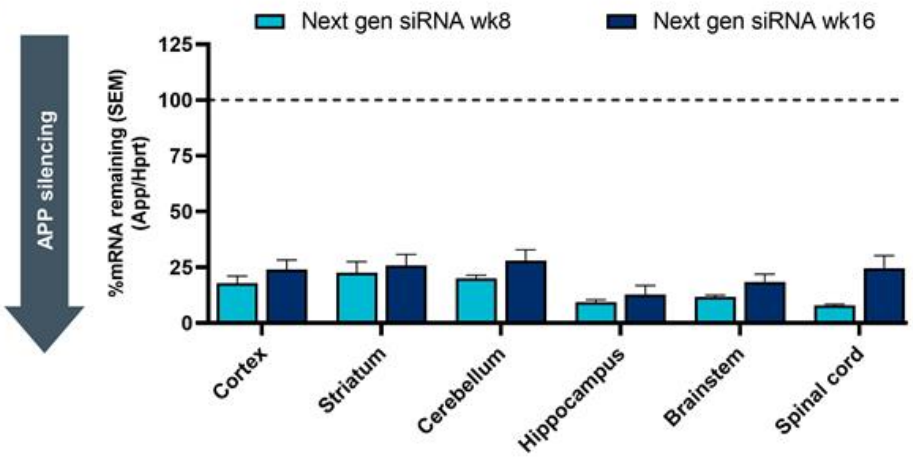
- Chemical impact
  - Introduction of neutral backbone
  - Unique structural feature of PN, specifically guanidine
  - Increased lipophilicity
  - Stereochemistry

- Extra-hepatic delivery
  - Titrating siRNA lipophilicity tunable PNs (PN variants)
  - Maintaining high Ago2 loading and intracellular trafficking
  - Titrating plasma protein binding
  - Altered delivery, enhanced potency and durability in various tissues

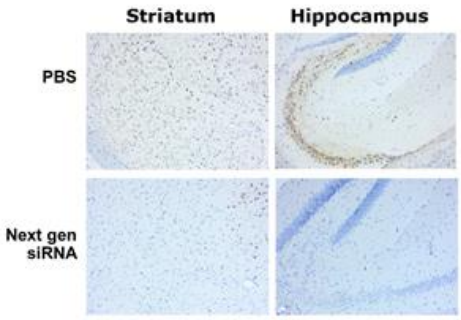


PN can tune extra-hepatic delivery of siRNA using rational design, including placement, number of modifications and PN variants

Single dose of next generation siRNA delivers broad, potent and durable CNS target engagement



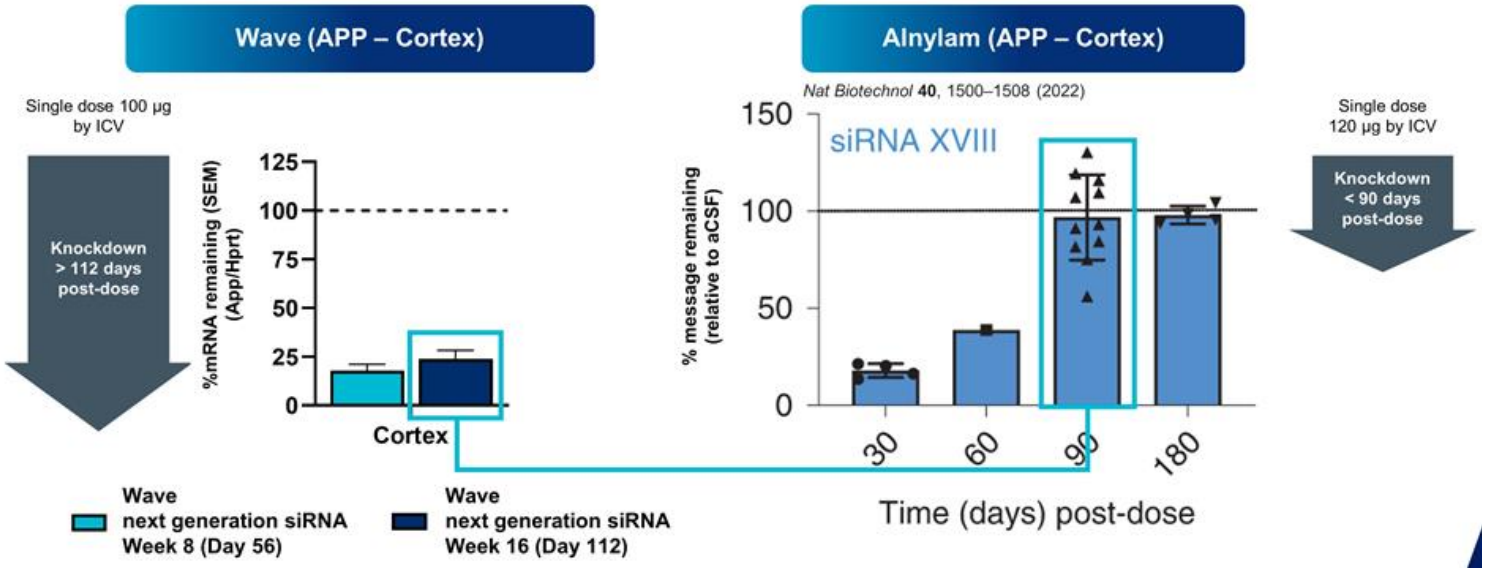
Robust target engagement translates to substantial App protein reduction across brain regions 8-weeks post single dose



Sustained APP knockdown of at least 75% throughout the 16-week study *in vivo* in mice

PBS (dotted line) or 100 µg of App siRNA administered ICV (n=7). PCR assays for RNA PD, relative fold changes of *App* to *Hprt* mRNA normalized to % of PBS; Stats: Three-way ANOVA followed by Bonferroni-adjusted post hoc test comparing condition to PBS (data not shown). Next gen siRNA significantly lower than PBS at both time points for all tissues at $P < 0.0001$ level; Immunohistochemical analysis of FFPE Mouse Brain tissue labeling App protein (Color Brown) with CS#19389 followed by a ready to use Polymer-HRP 2nd Detection antibody. Nuclei were counterstained with Hematoxylin (Color Blue). Single 100 ug ICV injection

Wave siRNA demonstrates more potent and durable silencing as compared to published state-of-the-art



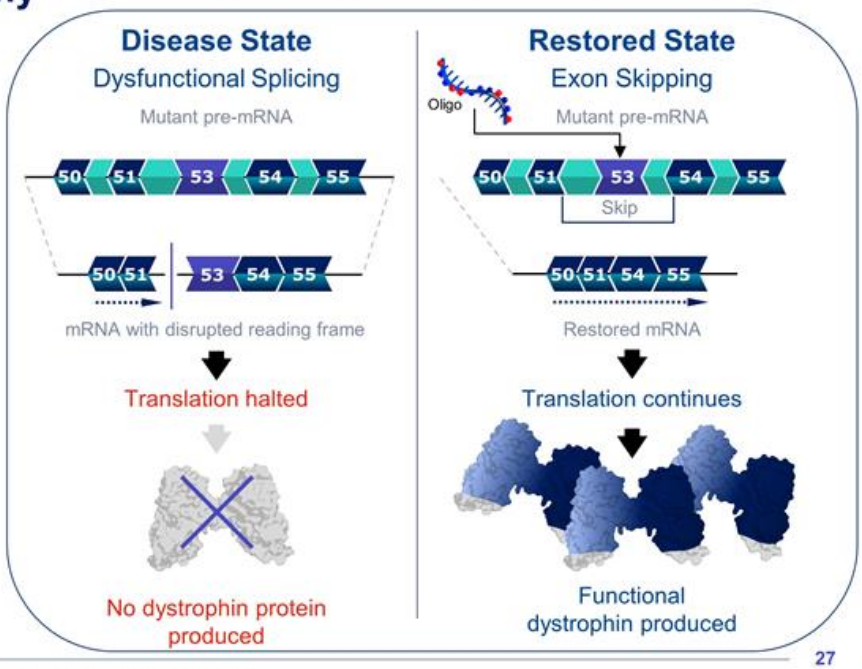
PBS (dotted line) or 100 µg of App siRNA administered ICV (n=7). PCR assays for RNA PD, relative fold changes of App to Hprt mRNA normalized to % of PBS; Stats: Three-way ANOVA followed by Bonferroni-adjusted post hoc test comparing condition to PBS (data not shown). Next gen siRNA significantly lower than PBS at both time points for all tissues at $P < 0.0001$ level. Source: Brown, K.M., Nair, J.K., Janas, M.M. et al. Expanding RNAi therapeutics to extrahepatic tissues with lipophilic conjugates. Nat Biotechnol 40, 1500–1508 (2022).

WVE-N531 (splicing)

Duchenne muscular dystrophy

Duchenne muscular dystrophy

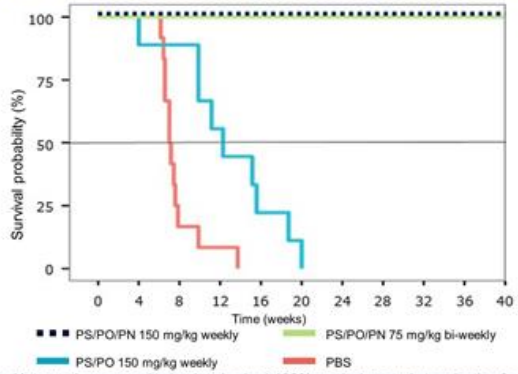
- **Genetic mutation in dystrophin gene prevents the production of dystrophin protein**, a critical component of healthy muscle function
- **Impacts approx. 1 in every 5,000 newborn boys each year**; approx. 20,000 new cases annually worldwide
  - Approx. 8-10% are amenable to exon 53 skipping
- **Dystrophin protein established by FDA as surrogate endpoint** reasonably likely to predict benefit in boys[1] for accelerated approval in DMD
- Increasing amount of functional dystrophin expression over minimal amount shown with approved therapies is expected to result in greater benefit for boys with DMD



[1]Vyondys: www.fda.gov; viltepso; www.fda.gov; Exondys; www.fda.gov; Amondys: www.fda.gov

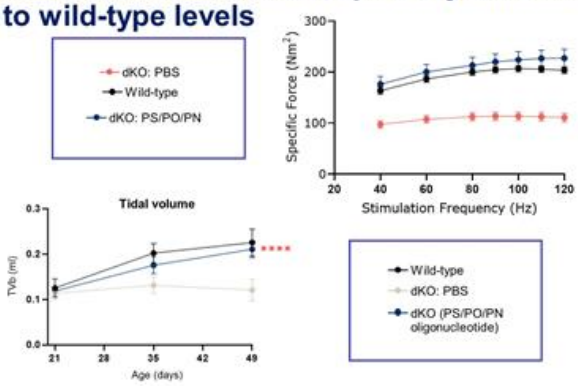
Extended survival in dKO preclinical model supports potential of Wave's PN-modified exon-skipping therapeutics for DMD

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

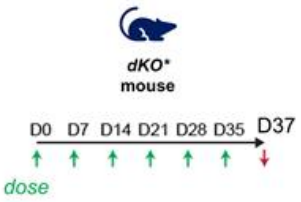


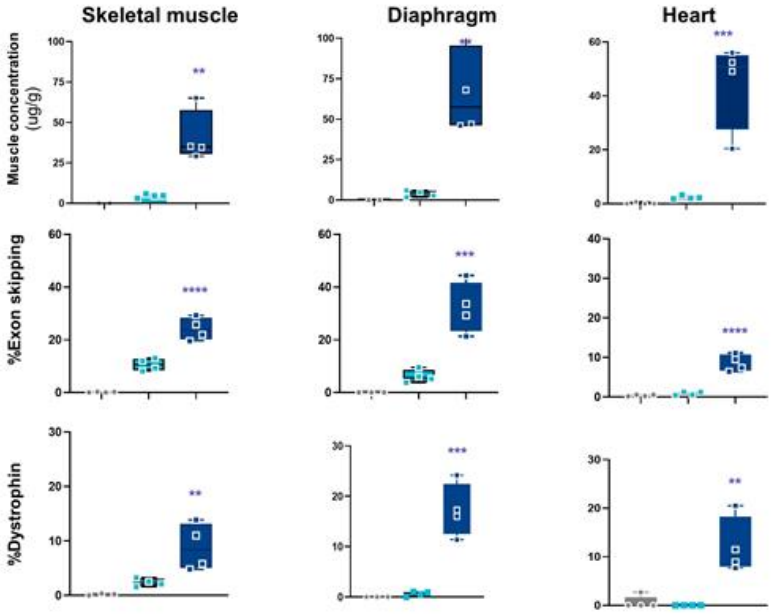
PN chemistry improved function and survival in dKO mice

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



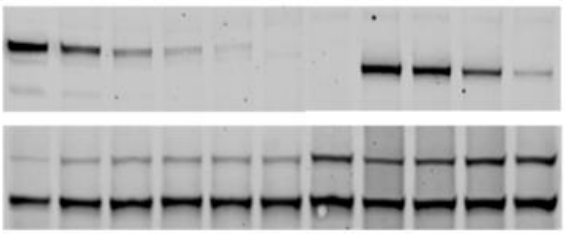


Kandasamy et al., 2022 Nuc Acids Res doi: 10.1093/nar/gkac018

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%



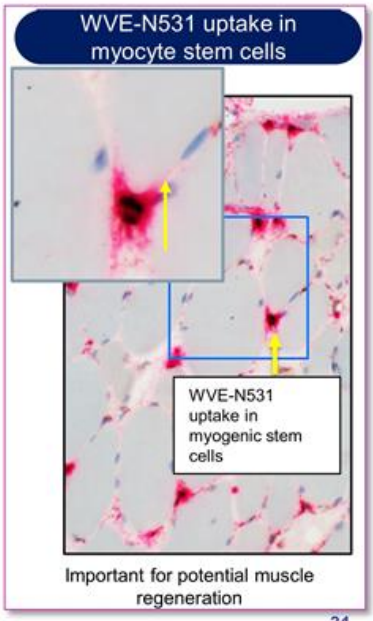
WVE-N531 reached high concentrations in heart and diaphragm in NHP

	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

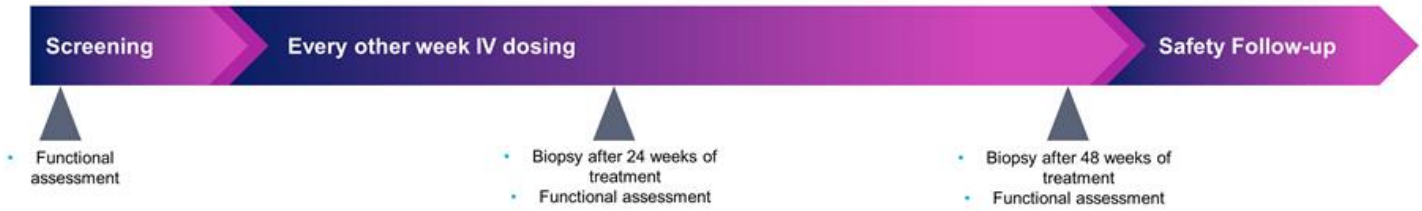
Clinical data from WVE-N531 Part A: High exon-skipping & muscle concentrations after three doses every other week

	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

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



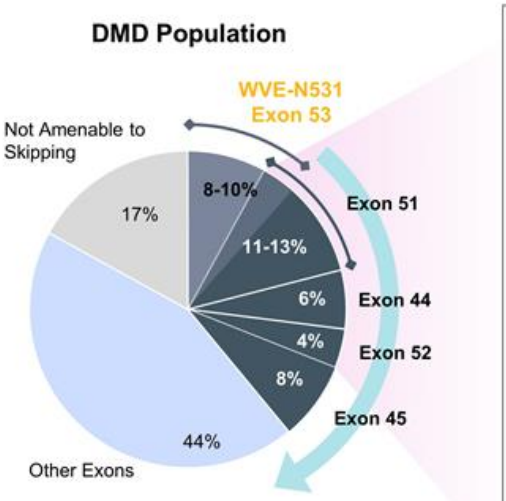
- Design of FORWARD-53: Phase 2, open-label, 10 mg/kg every other week
- Endpoints: Dystrophin (powered for >5% of normal), safety/tolerability, pharmacokinetics, digital and functional assessments (incl. NSAA and others)
- Muscle biopsies to assess dystrophin expression
- Fully enrolled (n=11) and dosing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

FORWARD-53

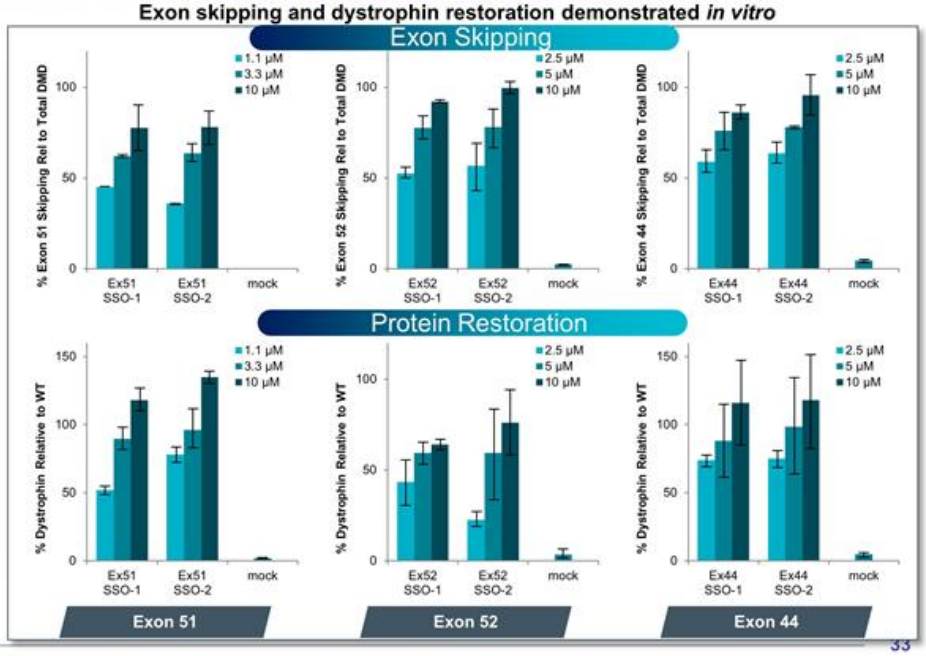
Potentially registrational 24-week dystrophin expression data are expected in 3Q 2024

IV: intravenous; NSAA: North star ambulatory assessment

Potential for Wave to address up to 40% of DMD population



Exon skipping and dystrophin restoration demonstrated *in vitro*



Left: Aartsma-Rus, et al. 2009 Hum Mutat 30, 293.

WVE-003
(antisense silencing)

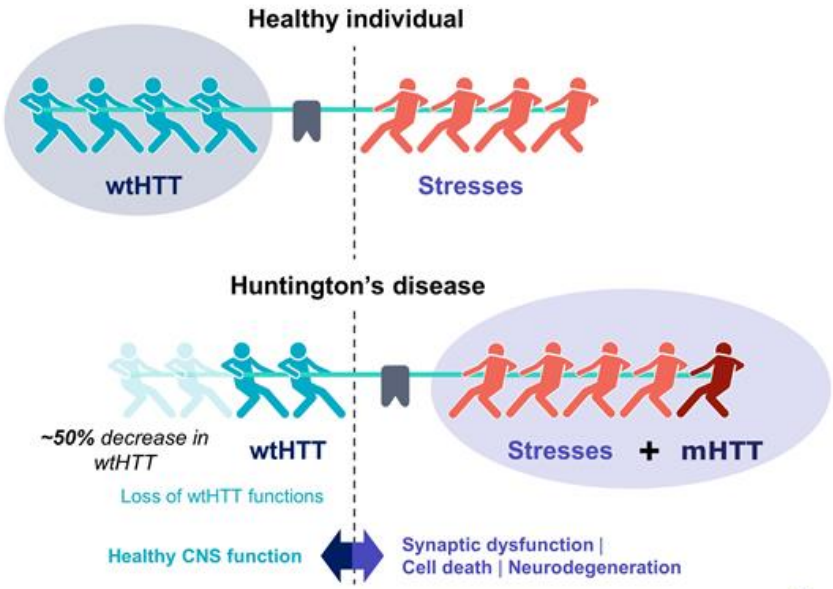
Huntington's Disease

WAVE LIFE SCIENCES

mHTT toxic effects lead to neurodegeneration; loss of wtHTT functions may also contribute to HD

Huntington's disease (HD)

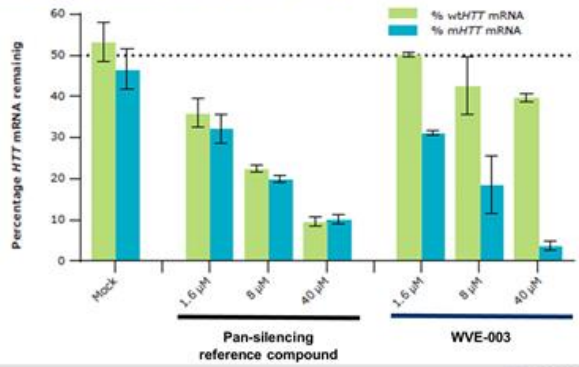
- Wild-type HTT (wtHTT) is critical for normal neuronal function[1]
- Expanded CAG triplet repeat in HTT gene results in production of mutant huntingtin protein (mHTT)
- HD is a monogenic autosomal dominant genetic disease; fully penetrant and affects entire brain
- Fatal disease characterized by cognitive decline, psychiatric illness, and chorea
- 30,000 people with HD in the US and more than 200,000 at risk of developing HD



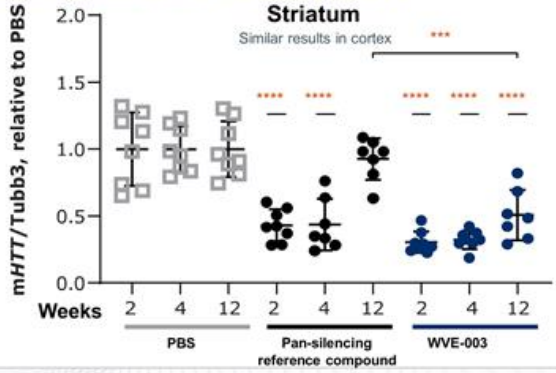
1 – Sources on wtHTT: 1. Leavitt 2006 2. Cattaneo 2005 3. Kumar 2016 4. Franco-Iborra 2020 5. Hamilton 2015 6. Ochaba 2014 7. Wong 2014 8. Rui 2015 9. Caviston 2007 10. Twelvetrees 2010 11. Strehlow 2007 12. Milnerwood 2010 13. Smith-Dijak 2019 14. Tousley 2019 15. Zhang 2018 16. McAdam 2020 17. Altar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

WVE-003 (SNP3) demonstrates selective, potent, and durable reduction of mHTT in preclinical models

Selectively reduces mHTT mRNA in HD iPSC neurons in vitro



Durable striatal mHTT knockdown for 12 weeks in BACHD mouse model

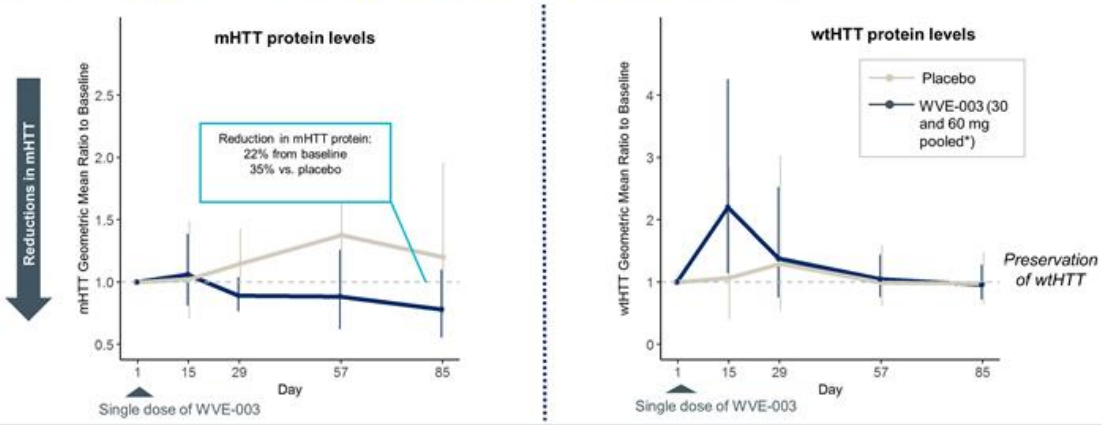


NHP study demonstrating significant tissue exposure levels of WVE-003 in deep brain regions resulted in $7 million milestone payment from Takeda in 4Q 2023

Results from ND50036 iPSC-derived medium spiny neurons. Total HTT knockdown quantified by qPCR and normalized to HPRT1. Oligonucleotide or PBS [100 µg ICV injections through cannula on days 1, 3, 5] delivered to BACHD transgenic. Mean ± SD (n=8, *P<0.0332, ***P<0.0002, ****P<0.0001 versus PBS unless otherwise noted). HPRT1, hypoxanthine-guanine phosphoribosyl transferase; iPSC, induced pluripotent stem cell; ICV, intracerebroventricular; PBS, phosphate-buffered saline

WVE-003: First-in-class allele-selective candidate for HD

Reductions in mean CSF mHTT and preservation of wtHTT observed in pooled analysis of single-dose cohorts in SELECT-HD clinical study

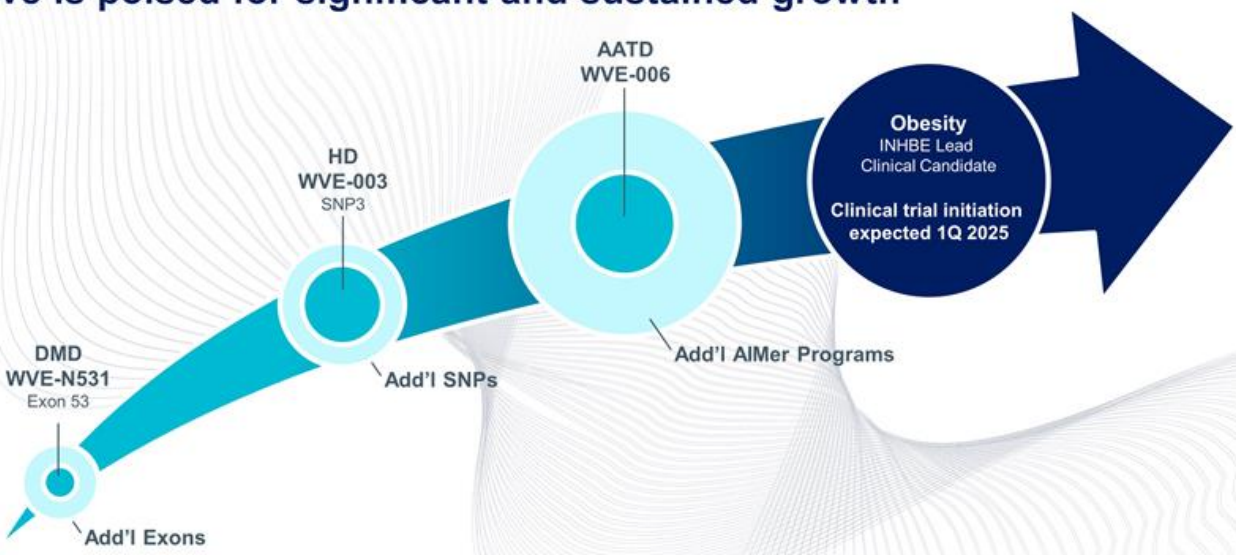


Data from 30 mg multi-dose cohort with extended follow-up, along with all single-dose data, expected 2Q 2024

mHTT: mutant huntingtin protein; wtHTT: wild-type huntingtin protein
*Pooled considering no apparent dose response between 2 single-dose cohorts; Data cut-off: August 29, 2022

Anticipated upcoming milestones

Wave is poised for significant and sustained growth



Clinical data in 2024 and advancement of INHBE candidate unlock potential to address > 50M patients in US and Europe

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 RNA editing candidate & potential best-in-class approach for AATD*	**2024:** Deliver proof-of-mechanism data from RestorAATion clinical program
INHBE lead clinical candidate (Obesity) *Driven by protective LoF variants in human genetics, potential next-gen therapeutic for obesity*	✓ Selected INHBE lead clinical candidate, with clinical trial application (CTA) expected as early as year-end 2024 **1Q 2025:** Initiate clinical trial for INHBE candidate
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 mHTT lowering, wtHTT-sparing approach*	**2Q 2024:** Deliver data from 30 mg multi-dose cohort with extended follow up, along with all single-dose data

Potential for significant cash inflows in 2024 from collaboration milestones from GSK and Takeda

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

WAVE™
LIFE SCIENCES

Reimagine possible.

For questions contact:
investorrelations@wavelifesci.com