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): May 3, 2023

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 May 3, 2023, Wave Life Sciences Ltd. (the "Company") announced its financial results for the quarter ended March 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 May 3, 2023, 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 May 3, 2023
99.2	Corporate Presentation of Wave Life Sciences Ltd. dated May 3, 2023
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/ Paul B. Bolno, M.D.*
Paul B. Bolno, M.D.
President and Chief Executive Officer

Date: May 3, 2023

Wave Life Sciences Reports First Quarter 2023 Financial Results and Provides Business Update

Emerging leader in RNA medicines with multi-modal discovery and development platform and first-in-class RNA editing programs

Rapidly advancing toward 2023 CTA submissions and first-in-human study for WVE-006, the industry's first RNA editing clinical candidate

Planning for potentially registrational Phase 2 clinical study for WVE-N531 to assess functional dystrophin protein restoration in DMD patients, following best-in-class exon-skipping data reported in December 2022

Preparing broad suite of first- and best-in-class medicines enabled by multi-modal RNA medicine platform and proprietary genetic insights from GSK collaboration; investor event anticipated in 3Q 2023

Cash and cash equivalents of $207.6 million as of March 31, 2023, with runway expected into 2025, plus potential milestone payments from GSK collaboration in 2023 and beyond

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

CAMBRIDGE, Mass., May 3, 2023 — Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced financial results for the first quarter ended March 31, 2023 and provided a business update.

"The first quarter of 2023 was marked by the launch of our transformational collaboration with GSK, which we believe will allow us to build substantial patient and shareholder value by expanding and accelerating our pipeline with capital, clinical capability, and proprietary genetic insights. This collaboration, which provided $170 million in upfront cash and equity, has the potential to provide additional cash milestones in 2023 and beyond. We are expeditiously progressing the industry's first RNA editing candidate, WVE-006, toward CTA submissions for alpha-1 antitrypsin deficiency, with the goal of early clinical proof-of-concept via measurement of validated serum surrogate markers in a clinical trial. In the first quarter, we also prepared for the launch of a potentially registrational Phase 2 study of WVE-N531 for boys with DMD, which is a program we believe may provide an important therapeutic option for them," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We are well-capitalized through our existing cash and potential near-term milestones to deliver on a steady cadence of clinical data across 2023 and 2024. Additionally, using our clinically validated multi-modal RNA medicines platform, we are preparing the next set of development programs that leverage our unique RNA editing, splicing, and knockdown capabilities. In the third quarter of this year, we plan to hold an investor event, during which we will demonstrate how we are continuing to extend our leadership in RNA editing and share preclinical data on new programs."

Recent Business Highlights

- **Presented WVE-N531 clinical data at MDA Conference; progressing WVE-N531 to Phase 2 clinical trial to evaluate functional dystrophin protein production in boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping.** In March 2023, at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference, Wave presented encouraging data from the initial cohort of the proof-of-concept open-label study of WVE-N531 to neuromuscular disease clinicians for the first time. Data for WVE-N531 included observation of best-in-class exon skipping and high muscle concentrations, while appearing safe and well-tolerated. A potentially registrational Phase 2 trial of WVE-N531 is planned, which will be powered to evaluate functional dystrophin expression following 24 and 48 weeks of biweekly dosing of WVE-N531. The primary endpoint will be dystrophin protein levels, and the study will also evaluate safety and tolerability, pharmacokinetics, and functional endpoints. Data are expected in 2024. If successful, WVE-N531 has potential to become a near-term wholly-owned commercial opportunity for Wave and would enable accelerated development of additional exon skipping candidates for other mutations.
- **Collaboration activities with GSK underway.** Wave's strategic collaboration with GSK, to advance transformative RNA medicines using Wave's multi-modal RNA platform, became effective in January 2023 and multiple target validation programs are already underway. The collaboration is designed to provide multiple value drivers to Wave, including maximizing the commercial opportunity for WVE-006 in alpha-1 antitrypsin deficiency (AATD), expanding Wave's pipeline with new targets leveraging unique genetic insights from GSK, and continuing opportunities to strengthen Wave's balance sheet.
- **Advancing WVE-006, a first-in-class RNA editing therapeutic for AATD, towards CTA submissions.** At multiple scientific conferences in the first quarter of 2023, Wave highlighted the preclinical data supporting WVE-006, its GalNAc-conjugated candidate for AATD. WVE-006 is Wave's first A-to-I(G) RNA base editing ("AIMer") development candidate, which is also first-in-class in AATD, and is uniquely designed for restoration of both healthy hepatic and pulmonary function with the opportunity for reversibility and a favorable safety profile. IND enabling studies for WVE-006 continue to advance and Wave is on track to submit clinical trial applications (CTAs) in the second half of 2023.
- **Presented leading RNA editing capability at Gordon Research Conference.** In March 2023, at the RNA Editing 2023 Gordon Research Conference, Wave presented an overview of its therapeutic base editing platform, including its novel base modifications and improvements in editing activity with optimized designs.

Recent Scientific Publications

- In April 2023, preclinical data for the company's novel siRNA formats were published in the journal of Nucleic Acids Research. The preclinical data demonstrated unprecedented, best-in-class Ago2 loading following administration of a single subcutaneous GalNAc-siRNA dose, leading to improved potency and durability *in vivo* versus comparator siRNA formats. Wave's RNAi capability is one of multiple modalities being advanced through the strategic research collaboration with GSK. All of Wave's publications can be viewed here.

Anticipated Upcoming Milestones and Events

WVE-N531 for DMD:

- Initiate dosing in Part B of WVE-N531 potentially registrational Phase 2 clinical trial in 2023
- Deliver data from Part B in 2024

WVE-006 for AATD:

- Submit CTAs for first-in-human study in 2H 2023

WVE-003 for HD:

- Deliver additional single-dose and multi-dose biomarker and safety clinical data in 2H 2023
- The update in expected timing for HD single-dose clinical data is due to a publicly announced cyber-attack that took place at Wave's mHTT assay vendor in April 2023. No Wave data or patient samples were impacted by the attack and Wave remains in close contact with the vendor as they address this issue.

WVE-004 for ALS/FTD:

- Deliver additional single- and multi-dose biomarker and safety clinical data in 1H 2023

Platform and Pipeline:

- Anticipate virtual investor event to be held in the third quarter of 2023 during which Wave will demonstrate how it is continuing to extend its leadership in RNA editing and share preclinical data on new wholly-owned programs
- Advance collaboration activities with GSK, with potential for additional cash inflows in 2023 and beyond

First Quarter 2023 Financial Results

Wave reported a net loss of $27.4 million in the first quarter of 2023, as compared to $37.8 million in the same period in 2022. The decrease in net loss year-over-year was primarily driven by revenue earned under the company's collaboration with GSK, which became effective January 27, 2023. Revenue earned under the GSK and Takeda collaborations in the first quarter of 2023 was $12.9 million. During the first quarter of 2022, revenue of $1.8 million was primarily earned under the Takeda collaboration.

Research and development expenses were $31.0 million in the first quarter of 2023, as compared to $27.5 million in the same period in 2022. The increase in research and development expenses was primarily due to increased external expenses related to Wave's clinical programs, as well as compensation-related expenses driven by growth to support the company's programs.

General and administrative expenses were $12.2 million in the first quarter of 2023, as compared to $12.4 million in the same period in 2022, primarily due to a decrease in compensation-related expenses.

As of March 31, 2023, Wave had $207.6 million in cash and cash equivalents, as compared to $88.5 million as of December 31, 2022. The company expects that its current cash and cash equivalents will be sufficient to fund operations into 2025.

Investor Conference Call and Webcast

Wave will host an investor conference call today at 8:30 a.m. ET to review first quarter 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-and-presentations. 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 clinical-stage RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases. Wave aspires to develop best-in-class medicines across multiple therapeutic modalities using PRISM, the company's proprietary discovery and drug development platform that enables the precise design, optimization, and production of stereopure oligonucleotides. Driven by a resolute sense of urgency, the Wave team is targeting a broad range of genetically defined diseases so that patients and families may realize a brighter future. To find out more, please visit www.wavelifesciences.com and follow Wave on Twitter @WaveLifeSci.

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 of data and completion of our clinical trials, 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 compared to others; our ability to design compounds using multiple modalities and the anticipated benefits of that approach; the breadth and versatility of PRISM; 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 status and progress of our programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; the benefit of nucleic acid therapeutics 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 any potential global macro events beyond our control 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)

	March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 207,562	$ 88,497
Prepaid expenses	9,231	7,932
Other current assets	2,798	2,108
Total current assets	219,591	98,537
Long-term assets:		
Property and equipment, net of accumulated depreciation of $39,197 and $37,846 as of March 31, 2023 and December 31, 2022, respectively	16,005	17,284
Operating lease right-of-use assets	25,838	26,843
Restricted cash	4,660	3,660
Other assets	1,176	62
Total long-term assets	47,679	47,849
Total assets	$ 267,270	$ 146,386
Liabilities, Series A preferred shares and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 11,906	$ 16,915
Accrued expenses and other current liabilities	7,622	17,552
Current portion of deferred revenue	106,960	31,558
Current portion of operating lease liability	6,078	5,496
Total current liabilities	132,566	71,521
Long-term liabilities:		
Deferred revenue, net of current portion	130,820	79,774
Operating lease liability, net of current portion	30,534	32,118
Other liabilities	190	190
Total long-term liabilities	161,544	112,082
Total liabilities	$ 294,110	$ 183,603
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at March 31, 2023 and December 31, 2022	$ 7,874	$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 98,104,844 and 86,924,643 shares issued and outstanding at March 31, 2023 and December 31, 2022, respectively	$ 837,886	$ 802,833
Additional paid-in capital	122,192	119,442
Accumulated other comprehensive income (loss)	(50)	(29)
Accumulated deficit	(994,742)	(967,337)
Total shareholders' equity (deficit)	$ (34,714)	$ (45,091)
Total liabilities, Series A preferred shares and shareholders' equity (deficit)	$ 267,270	$ 146,386

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

(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2023	2022
Revenue	$ 12,929	$ 1,750
Operating expenses:		
Research and development	30,979	27,470
General and administrative	12,235	12,374
Total operating expenses	43,214	39,844
Loss from operations	(30,285)	(38,094)
Other income, net:		
Dividend income and interest income, net	1,873	26
Other income, net	1,007	254
Total other income, net	2,880	280
Loss before income taxes	(27,405)	(37,814)
Income tax provision	—	—
Net loss	$ (27,405)	$ (37,814)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.27)	$ (0.62)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	102,056,712	60,516,616
Other comprehensive loss:		
Net loss	$ (27,405)	$ (37,814)
Foreign currency translation	(21)	(86)
Comprehensive loss	$ (27,426)	$ (37,900)

Investor Contact:

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Alicia Suter
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Exhibit 99.2

Wave Life Sciences
Corporate Presentation

May 3, 2023

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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.

Emerging leader in RNA medicines

Multi-modal drug discovery and development platform to address new areas of disease biology
RNA editing, splicing and silencing

Differentiated, clinical-stage RNA medicines pipeline with first-in-class RNA editing programs

Strategic collaborations to expand and advance pipeline (GSK and Takeda)

Multiple pipeline and platform catalysts expected in 2023 and beyond

Well-capitalized with expected cash runway into 2025

GMP manufacturing

Strong and broad IP position[1]

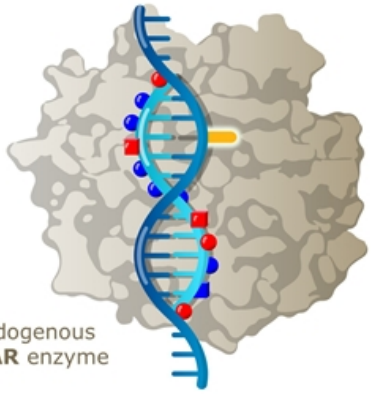
Wave Life Sciences is an RNA medicines company committed to delivering life-changing treatments for people battling devastating diseases

[1]stereopure oligonucleotides and novel backbone chemistry modifications

RNA medicines allow matching disease target to therapeutic modality

RNA Base Editing

- Efficient editing of RNA bases to **restore** or **modulate** protein production



Endogenous **ADAR** enzyme

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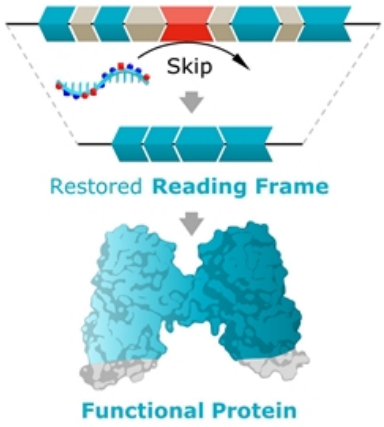
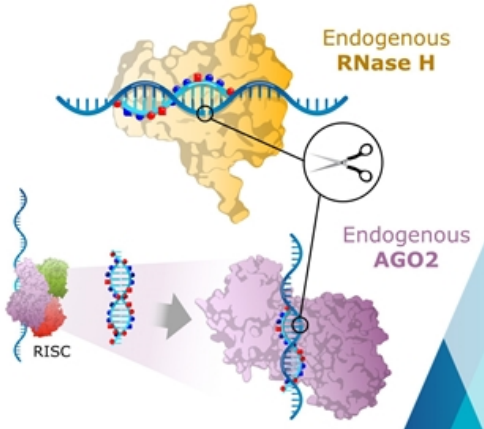
Splicing

- Restore RNA transcripts and **turn on** protein production



Silencing

- Degradation of RNA transcripts to **turn off** protein production



Robust RNA medicines pipeline with first-in-class RNA editing programs

Program	Discovery	Preclinical	Clinical	Rights	Patient population (US & Europe)
RNA EDITING					
WVE-006 SERPINA1 (AATD)				GSK exclusive global license	200K
Multiple undisclosed				100% global	-
SPLICING					
WVE-N531 Exon 53 (DMD)			Phase 1/2	100% global	2.3K
Other exons (DMD)				100% global	Up to 18K
SILENCING: ANTISENSE					
WVE-003 mHTT (HD)			Phase 1/2	Takeda 50:50 Option	25K Manifest (SNP3) 60K Pre-Manifest (SNP3)
WVE-004 C9orf72 (ALS and FTD)			Phase 1/2	Takeda 50:50 Option	4K (C9-ALS) 26K (C9-FTD)
SCA3 (ATXN3)				Takeda 50:50 Option	8K
SILENCING: RNAi					
Undisclosed				100% global	-

Through GSK collaboration, Wave can advance up to three collaboration programs and GSK can advance up to eight collaboration programs

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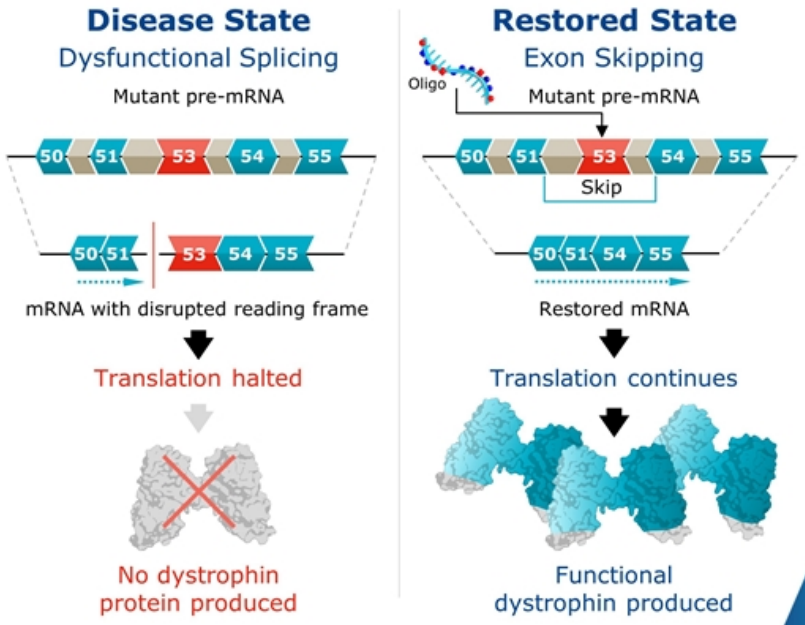
AATD: Alpha-1 antitrypsin deficiency; DMD: Duchenne muscular dystrophy; HD: Huntington's disease; ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; SCA3: Spinocerebellar ataxia 3

WVE-N531

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

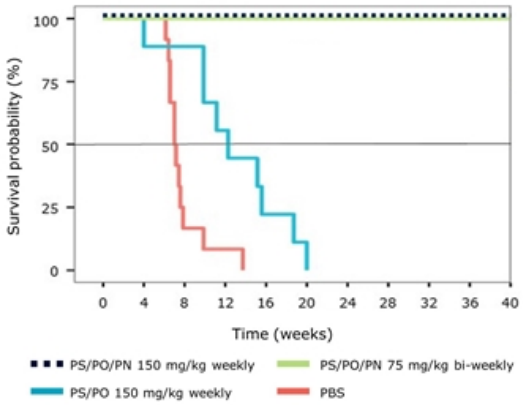


[1]Vyondys: www.fda.gov; viltepso; www.fda.gov; Exondys; www.fda.gov; Amondys: www.fda.gov

Preclinical data supported advancing WVE-N531 to clinical development

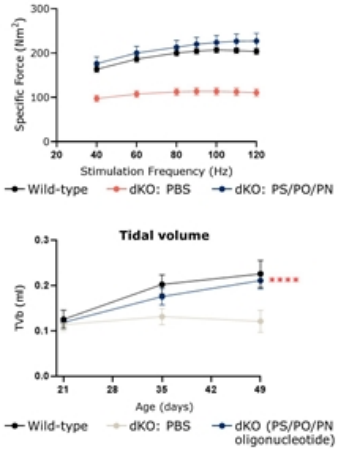
PN chemistry improved function and survival in dKO mice

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



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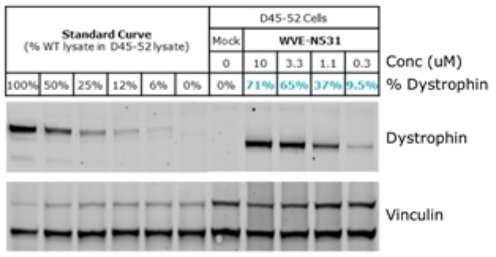
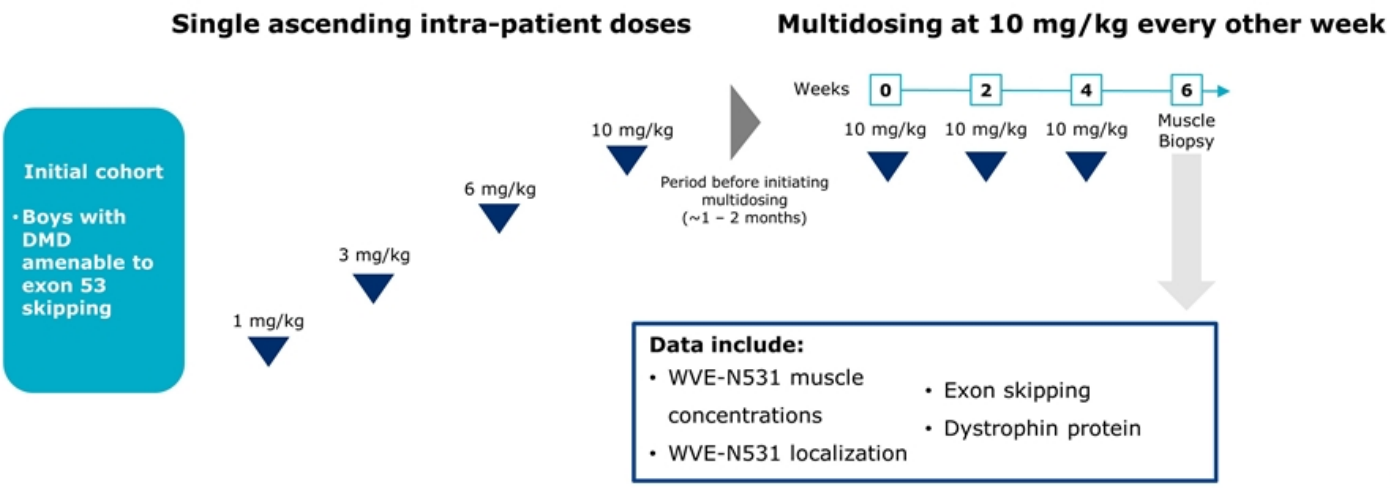
Kandasamy et al., 2022; doi: 10.1093/nar/gkac018

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

Western Blot normalized to primary healthy human myoblast lysate



In multidose portion of study, patients received three biweekly 10 mg/kg doses



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▼ Dose WVE-N531

WVE-N531 in DMD: Delivered positive proof-of-concept data in 4Q 2022

- High exon skipping and muscle concentrations after three biweekly 10 mg/kg doses
- Similar exon skipping regardless of mutation
  - Patient 1: del48-52
  - Patient 2: del45-52
  - Patient 3: del51-52
- PK analysis indicated 25-day half-life in plasma
- WVE-N531 appeared safe and well-tolerated

Patient	Tissue Source	Tissue concentration (µg/g)	% Exon skipping by RT-PCR	Dystrophin by Western blot (% of normal)
1	Deltoid	85.5	61.5	0.24
2	Deltoid	33.5	49.8	0.23
3	Bicep	8.3	47.9	0.34

Mean muscle concentration: 42 µg/g

Mean exon skipping: 53%

Mean dystrophin: 0.27% of normal (BLQ)

Data presented March 22, 2023 at Muscular Dystrophy Association Clinical and Scientific Conference

Biopsies collected ~2 weeks post-last dose (3 biweekly doses of 10 mg/kg)
Data cut-off: December 6, 2022

42 µg/g = 6.1 µM

BLQ: Below level of quantification (1%)

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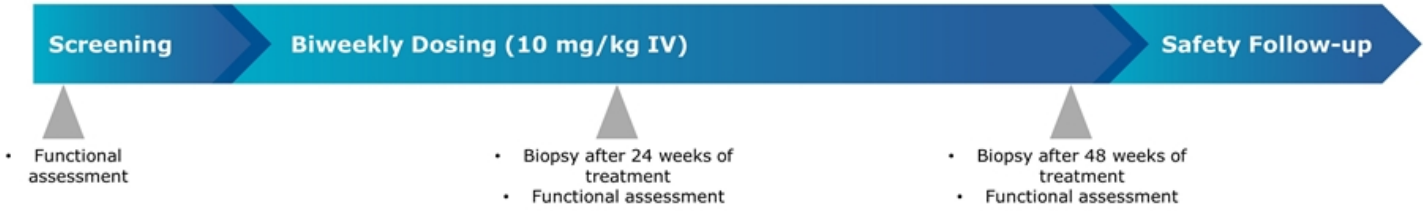
Initiating Part B, a potentially registrational Phase 2 clinical trial of WVE-N531



- **Design**: Phase 2, open-label, 10 mg/kg every other week, up to 10 patients
- **Endpoints**: Dystrophin (powered for >5% of normal), safety/tolerability, pharmacokinetics, functional assessments (incl. NSAA and others)
- **Biopsies**:
  - After 24 weeks of treatment
  - After 48 weeks of treatment
- **Data from Part B expected in 2024**

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IV: intravenous; NSAA: North star ambulatory assessment

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GSK Collaboration and WVE-006 for Alpha-1 antitrypsin deficiency (AATD)

Strategic collaboration with GSK to develop transformative RNA medicines for genetically defined diseases

- ✓ **$170 million upfront to Wave** (cash and equity[1])
- ✓ Additional research support funding
- ✓ Potential for **up to $3.3 billion in milestones**[2]
- ✓ Expands Wave's pipeline

Extends cash runway into 2025

PRISM

WAVE LIFE SCIENCES

Multiple value drivers to Wave

Milestone / royalties	Milestone / royalties	Genetic targets
GSK granted exclusive global license to WVE-006 for AATD	**GSK to advance up to eight collaboration programs**	**Wave to leverage GSK's genetic insights**
Up to $225 million in development and launch milestones	Up to $1.2 billion in aggregate in initiation, development and launch milestones	Wave to advance up to three wholly owned collaboration programs (or more pending agreement with GSK)[3]
Up to $300 million in sales-related milestones	Up to $1.6 billion in aggregate in sales-related milestones	
Double-digit tiered royalties as a percentage of net sales up to high-teens	Tiered royalties as a percentage of net sales up to low-teens	
Development and commercialization responsibilities transfer to GSK after completion of first-in-patient study	Development and commercialization responsibilities transfer to GSK at development candidate	
First-in-class RNA editing program	Collaboration leverages Wave's unique stereopure, PN-chemistry containing PRISM™ platform, including **editing**, **splicing**, **silencing** (RNAi and antisense)	

[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: Designed to correct mutant SERPINA1 transcript to address both liver and lung manifestations of AATD

WVE-006 designed to correct Z allele mRNA to enable M-AAT protein to be produced

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

WVE-006 (GalNAc-conjugated AIMer)

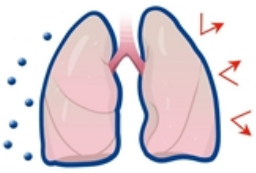
Edited *SERPINA1* mRNA enables wild-type M-AAT protein production

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

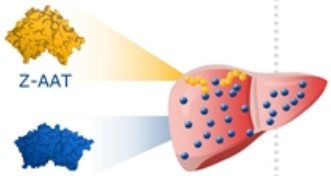
1) Restore circulating, functional wild-type M-AAT

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

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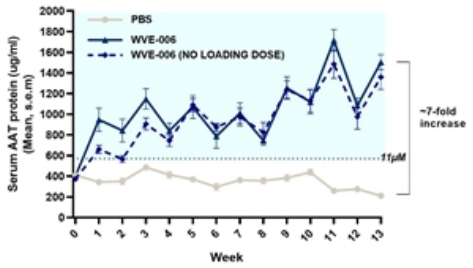
AAT: Alpha-1 antitrypsin Strnad *et al.*, 2020 *N Engl J Med* 382:1443-55; Blanco *et al.*, 2017 *Int J Chron Obstruct Pulmon Dis* 12:561-69; Remih *et al.*, 2021 *Curr Opin Pharmacol* 59:149-56.

WVE-006 in AATD: First-in-class RNA editing candidate approaching the clinic

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

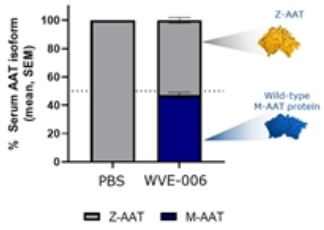
Increased AAT protein in NSG-PiZ mice

WVE-006 treatment results in serum AAT protein levels >11 uM in NSG-PiZ mice



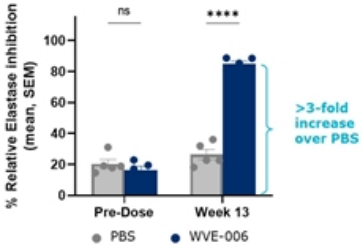
Confirmed restored wild-type M-AAT protein

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



CTA submissions for first-in-human study expected in 2H 2023

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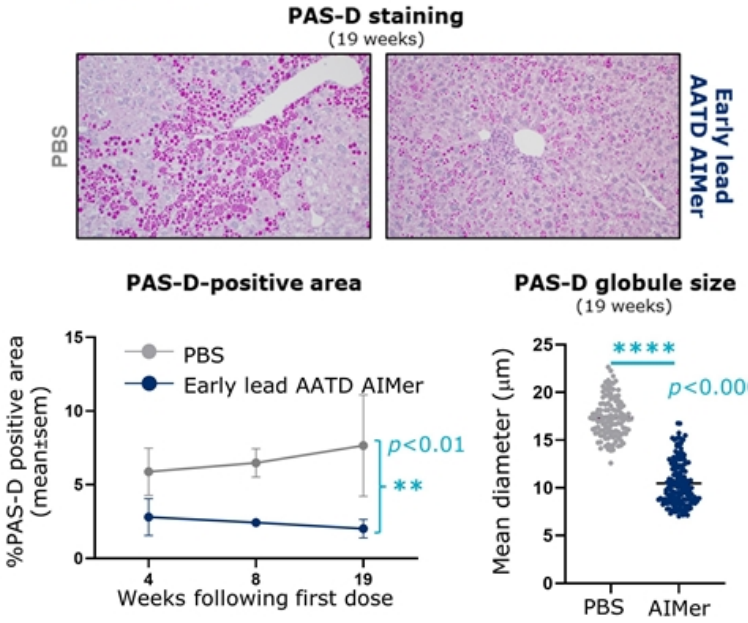
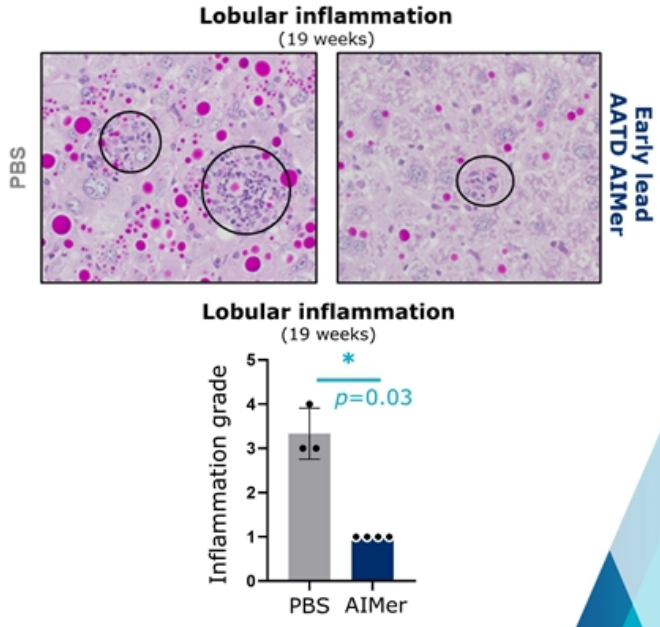
AATD: Alpha-1 antitrypsin deficiency; M-AAT protein: wild-type AAT protein; WVE-006 administered subcutaneously (10 mg/kg bi-weekly) in 7-week old NSG-PiZ mice (n=5 per group); Loading dose: 3 x 10 mg/kg at Day 0. Left: Liver biopsies collected at wk 13 (1 wk after last dose) and SERPINA1 editing quantified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

Early lead (pre-optimization) AATD AIMer reduces aggregation of Z-AAT and inflammation in mouse liver





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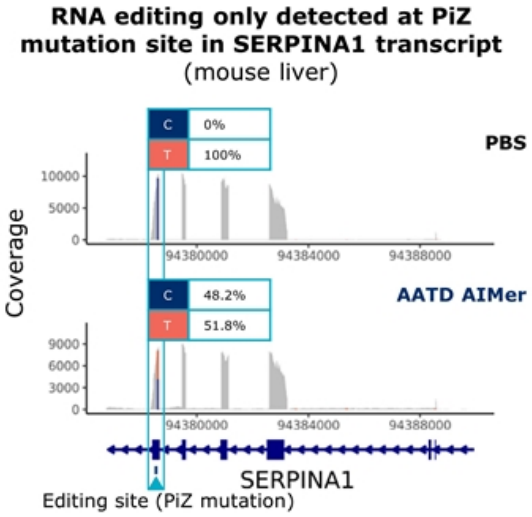
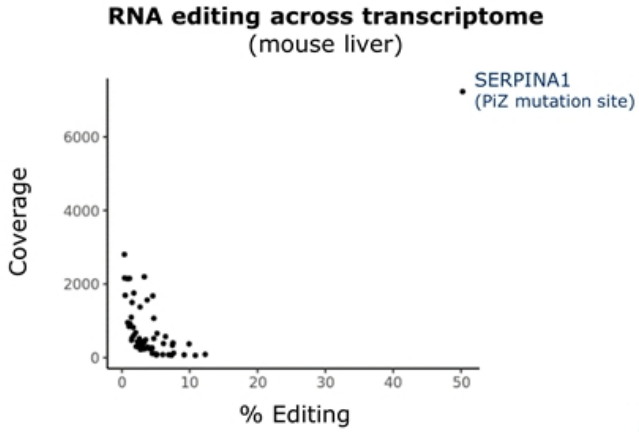
Early lead pre-optimization AATD AIMer (SA1-5) administered in hu*ADAR/SERPINA1* mice (8–10 wKs old); lower left: 20x liver images PAS-D stained, 19 weeks; Quantification of PAS-D positive staining, Stats 2-way ANOVA; Right: Quantification lobular inflammation grade (Grade based on # of inflammatory foci in lobules: Grade 0: 0; G1 1-5; G2 6-10; G3 11-15; G4 ≥16) and mean globular diameter (40 largest globules/ animal) with HALO. Stats Wilcox rank-sum tests

AIMer-directed editing is highly specific in mice

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

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WVE-004

Amyotrophic Lateral Sclerosis (ALS)

Frontotemporal Dementia (FTD)

C9orf72 repeat expansions: One of the most common genetic causes of ALS and FTD

Hexanucleotide (G_4C_2)- repeat expansions in C9orf72 gene are common autosomal dominate cause for ALS and FTD

Different manifestations across a clinical spectrum

Amyotrophic Lateral Sclerosis (ALS)	Frontotemporal Dementia (FTD)
• Fatal neurodegenerative disease	• Progressive neuronal degeneration in frontal / temporal cortices
• Progressive degeneration of motor neurons in brain and spinal cord	• Personality and behavioral changes, gradual impairment of language skills
• C9-specific ALS: ~2,000 patients in US	• C9-specific FTD: ~10,000 patients in US

Including patients with C9-associated ALS, FTD or both

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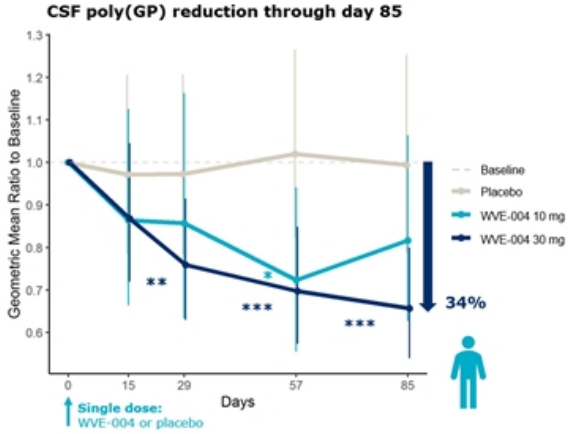
Sources: Balendra et al, EMBO Mol Med, 2017; Brown et al, NEJM, 2017, DeJesus-Hernandez et al, Neuron, 2011. Renton et al, Neuron, 2011. Zhu et al, Nature Neuroscience, May 2020, Stevens et al, Neurology 1998

WVE-004 in C9-ALS/FTD: Successful translation of preclinical data to clinic

- PK/PD modeling using preclinical *in vivo* models predicted pharmacodynamically active starting dose
- **Additional single- and multi-dose biomarker and safety clinical data expected in 1H 2023 from following cohorts:**
  - 20 mg single dose
  - 30 mg single dose
  - 60 mg single dose
  - 10 mg monthly dosing
  - 10 mg quarterly dosing

Target engagement in patients supported advancing FOCUS-C9 clinical study



PK: pharmacokinetic PD: pharmacodynamic; Right: Mixed model for repeated measures used to estimate geometric mean ratio to baseline via least squares mean and to calculate p-values. P-values represented by asterisks are for within-dose group geometric mean ratios. *p≤0.05, **p≤0.01, ***p≤0.001. Poly(GP) assay: Wilson et al., 2022 J Neurol Neurosurg Psychiatry doi:10.1136/jnnp-2021-328710. Data cut-off: March 24, 2022

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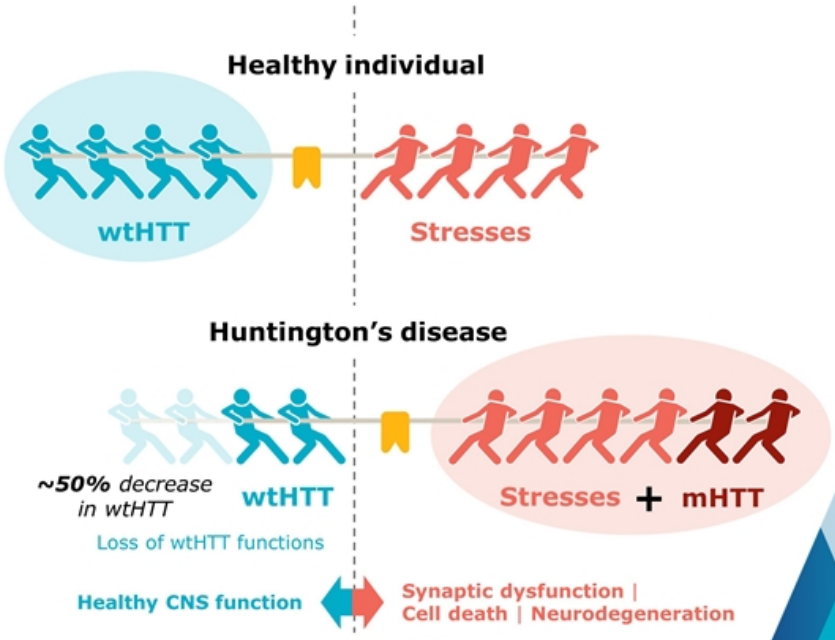
WVE-003

Huntington's Disease

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
- 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



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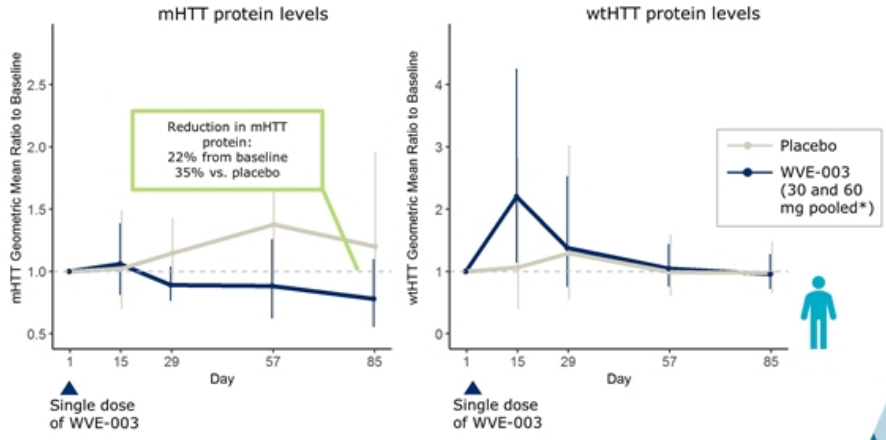
WVE-003: First-in-class allele-selective candidate for HD

- mHTT protein reductions observed in single dose cohorts (Sep. 2022)
- wtHTT protein levels appear consistent with allele-selectivity
- Generally safe and well-tolerated
- **Additional single-dose and multi-dose biomarker and safety clinical data expected in 2H 2023**

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



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

AIMers

RNA base editing capability

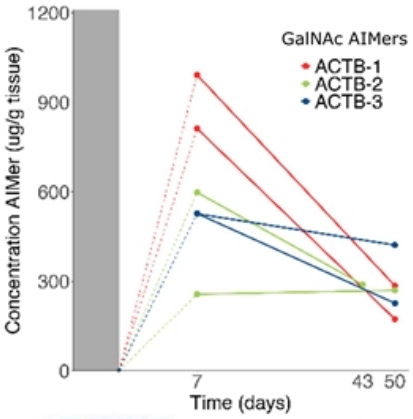
Proof-of-concept preclinical RNA editing data published in *Nature Biotechnology* (March 2022)

nature biotechnology ARTICLES

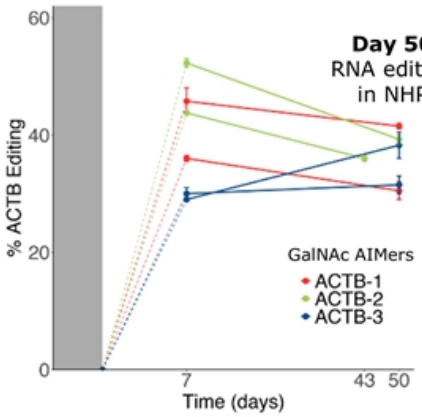
Endogenous ADAR-mediated RNA editing in non-human primates using stereopure chemically modified oligonucleotides

- Specificity *in vitro* & *in vivo* (NHPs)
- *In vitro-in vivo* translation (NHPs)
- GalNAc conjugation
- Foundational AIMer SAR

AIMers detected in liver of NHP at Day 50 (PK)

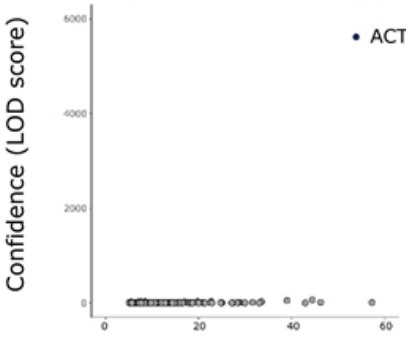


Substantial and durable editing in NHP liver *in vivo* (PD)



ADAR editing with ACTB AIMer is highly specific

RNA editing within full transcriptome (primary human hepatocytes)



RNA editing only detected at editing site in ACTB transcript

LIFE SCIENCES Monian et al., 2022 published online Mar 7, 2022; doi: 10.1038.s41587-022-01225-1
SAR structure-activity relationship

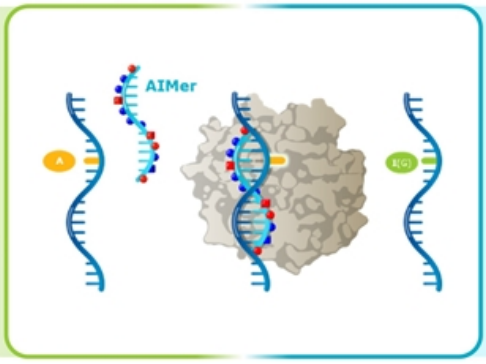
Expanding addressable disease target space using AIMers to activate pathways and upregulate expression

Correct G-to-A driver mutations with AIMers

Restore or correct protein function ☑

WVE-006 (GalNAc AIMer)
AATD

Modulate protein interactions with AIMers



- ☑ **Modulate protein-protein interaction** *Achieved POC*
- ☑ **Upregulate expression** *Achieved POC*
- ☐ Modify function
- ☐ Post-translational modification
- ☐ Alter folding or processing

AIMers provide dexterity, with applications beyond precise correction of genetic mutations, including upregulation of expression, modification of protein function, or alter protein stability

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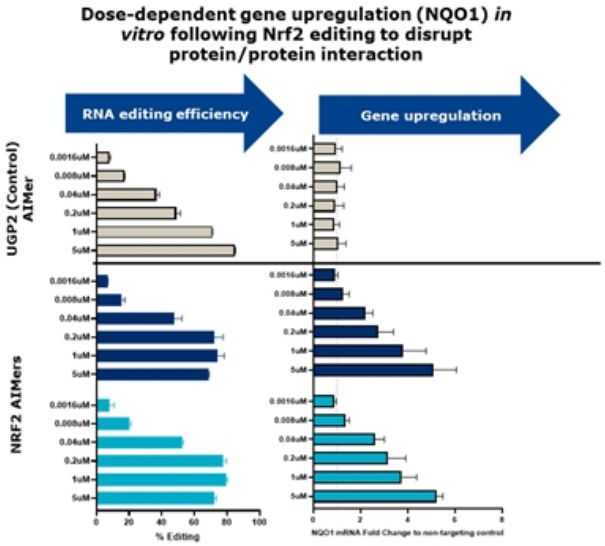
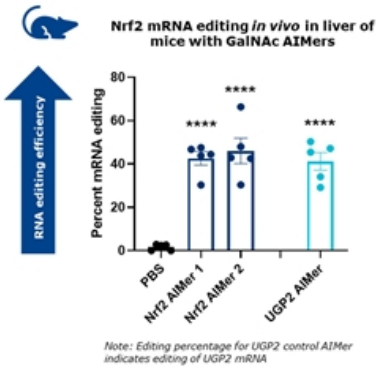
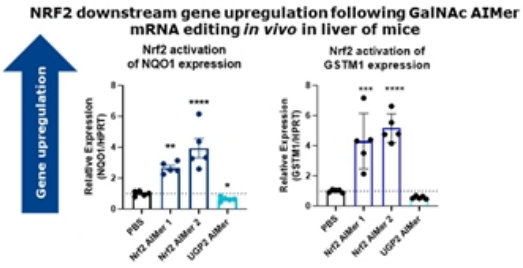
POC: proof of concept

Modulation of protein-protein interactions: AIMers enable activation of gene pathway *in vivo* with single edit





Note: Editing percentage for UGP2 control AIMer indicates editing of UGP2 mRNA



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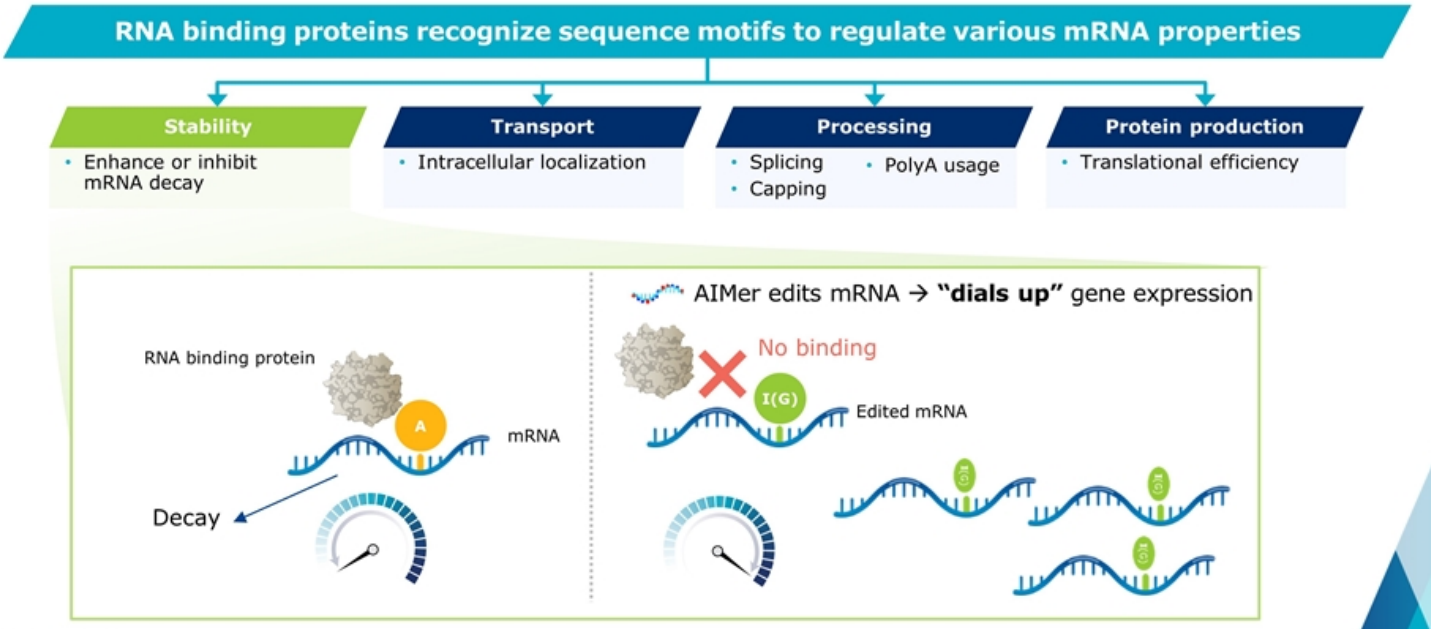
n=2; Primary hepatocytes 48h of treatment with the indicated dose concentration of AIMers

Upregulation: AIMers can edit RNA motifs to restore or upregulate gene expression



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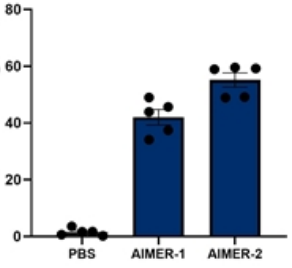
AIMers upregulate mRNA and downstream serum protein *in vivo* above anticipated threshold

Target A (undisclosed liver target)

- High unmet need with potential for multiple large indications
- Preserves endogenous protein function
- Serum protein with biomarkers of pathway activation
- Potential benefit 3-fold+ upregulation in mouse

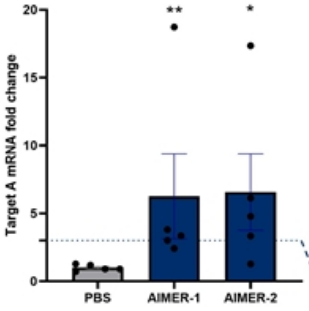
RNA editing

mRNA editing
7 days post-initial dose
GalNAc AIMer

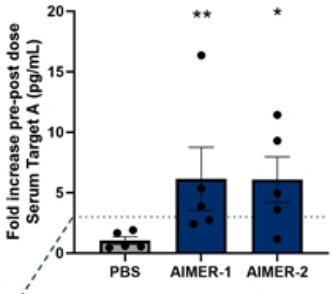


Upregulation

mRNA upregulation
7 days post-initial dose
GalNAc AIMer



Protein upregulation
7 days post-initial dose
GalNAc AIMer



Potential threshold for benefit

- ✓ *In vitro* to *in vivo* translation of mouse Target A mRNA upregulation
- ✓ *In vivo* mRNA upregulation corresponds to an upregulation of Target A protein in serum at Day 7 demonstrating proof-of-concept

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hADAR mouse dosed subcutaneously 3 x 10 mg/kg GalNAc-conjugated AIMer or PBS days (0, 2, 4), taken down at day 7

WAVE
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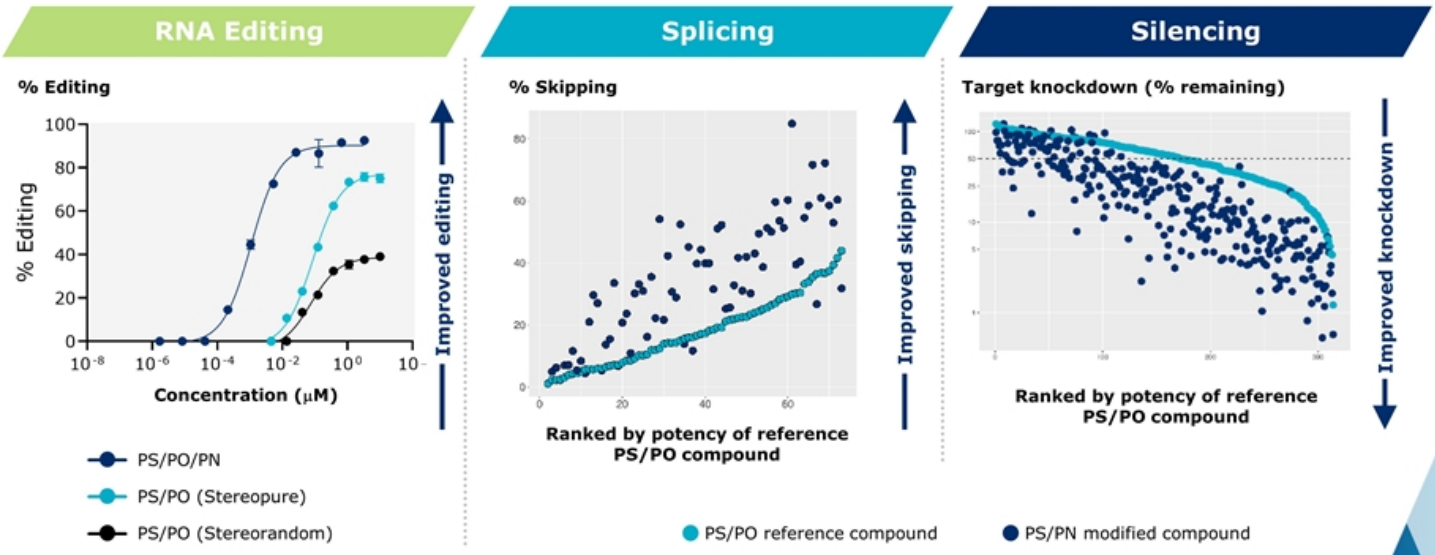
Wave's discovery and drug development platform

PRISM

Proprietary PN chemistry enhances potency across modalities



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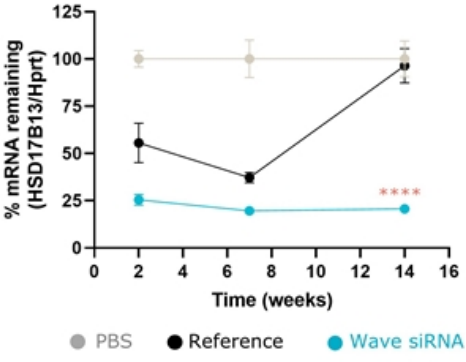
Left: Experiment was performed in iPSC-derived neurons *in vitro*; target mRNA levels were monitored using qPCR against a control gene (HPRT1) using a linear model equivalent of the ΔΔCt method; Middle: DMD patient-derived myoblasts treated with PS/PO or PS/PO/PN stereopure oligonucleotide under free-uptake conditions. Exon-skipping efficiency evaluated by qPCR. Right: Data from independent experiments

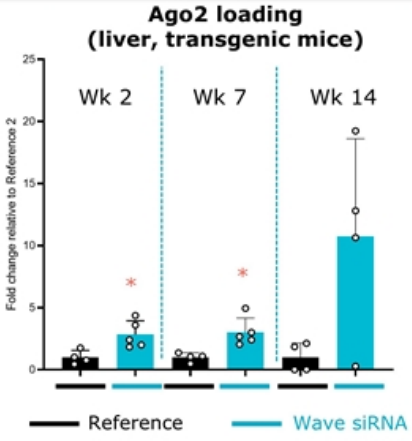
Potential for best-in-class RNAi enabled by Wave's PRISM platform

Nucleic Acids Research

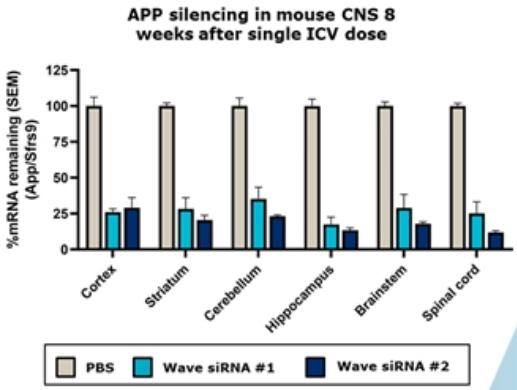
Impact of stereopure chimeric backbone chemistries on the potency and durability of gene silencing by RNA interference

- Unprecedented Ago2 loading following administration of single subcutaneous dose





- First in vivo study of unconjugated siRNAs demonstrated 70-90% APP silencing across six brain regions in mouse CNS at 8 weeks



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

WAVE LIFE SCIENCES

Left, Middle: Mice expressing human *HSD17B13* transgene treated (3 mg/kg)siRNA 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: ICV: Intracerebroventricular; APP: Amyloid precursor protein ; CNS: central nervous system; B6 mice were administered PBS or 100 µg of APP siRNA by ICV injection on day 0 (n=7). Mice euthanized 8 weeks after administration. Taqman qPCR assays used for RNA PD, relative fold changes of *App* to *Sfrs9* mRNA normalized to percentage of PBS group. All treated group show *P*≤0.0001 compared to PBS group in 2way ANOVA.

Delivering on pipeline and platform catalysts

RNA EDITING	SPLICING	ANTISENSE SILENCING	RNAi
WVE-006 for AATD *Most advanced RNA editing candidate & potential best-in-class approach for AATD* **WVE-006 CTA submissions expected in 2H 2023** **Expansion opportunities in liver, CNS and kidney**	**WVE-N531 for DMD** *Potential best-in-class approach with highest exon skipping reported* **Dosing in potentially registrational clinical trial expected in 2023; data expected in 2024** **Expansion opportunities in other exons, as well as other muscle diseases and CNS**	**WVE-003 for HD** *First-in-class wtHTT-sparing approach* **Data expected 2H 2023** **WVE-004 for ALS/FTD** *Variant-selective approach for C9orf72* **Data expected 1H 2023** **Enables discussion on next steps with Takeda**	**Newest modality in Wave platform** *Preclinical data suggest best-in-class potential for Wave RNAi capability* **Hepatic, CNS and beyond**

DISCOVERY PIPELINE & COLLABORATIONS

Anticipate investor event in 3Q 2023 during which Wave will demonstrate how it is continuing to extend its leadership in RNA editing and share preclinical data on new wholly-owned programs

Advance collaboration activities with GSK, with potential for additional cash inflows in 2023 and beyond

WAVE LIFE SCIENCES

Realizing a brighter future for people affected by genetic diseases

For more information:

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617.949.4827

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