Wave Life Sciences

42nd Annual J.P. Morgan Healthcare Conference

January 10, 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
2024 expected to be an inflection year that drives significant value

Recent achievements

- ✓ Dosed first-ever RNA editing therapeutic; extended leadership in RNA editing
- ✓ Best-in-class exon skipping program; initiated potentially registrational FORWARD-53 trial in DMD
- ✓ Clinically relevant mHTT allele-selective single dose knockdown, initiated SELECT-HD multi-dose cohort
- ✓ Announced next generation obesity program (INHBE siRNA) for fat loss, with muscle sparing
- ✓ Pipeline of additional RNA medicines to address rare and prevalent diseases
- ✓ $142M additional cash from Dec. ’23 offering and Q4 2023 milestones; runway Q4 2025*

Anticipated 2024 milestones

- Proof-of-mechanism data from RestorAATion clinical program of WVE-006 for AATD in 2024
- Select INHBE clinical candidate for obesity in 3Q 2024
- 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

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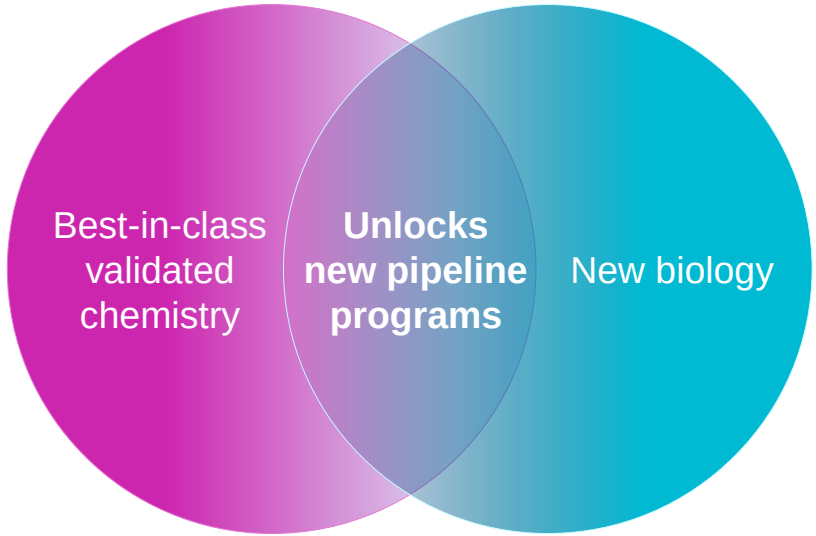
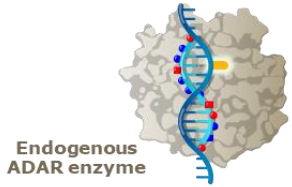
*Cash runway does not include potential future milestones or opt-in payments under GSK and Takeda collaborations

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

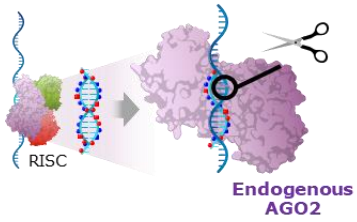


- Accessing new endogenous enzymes for novel modalities (RNA editing)
- Opening up new targets, including prevalent diseases

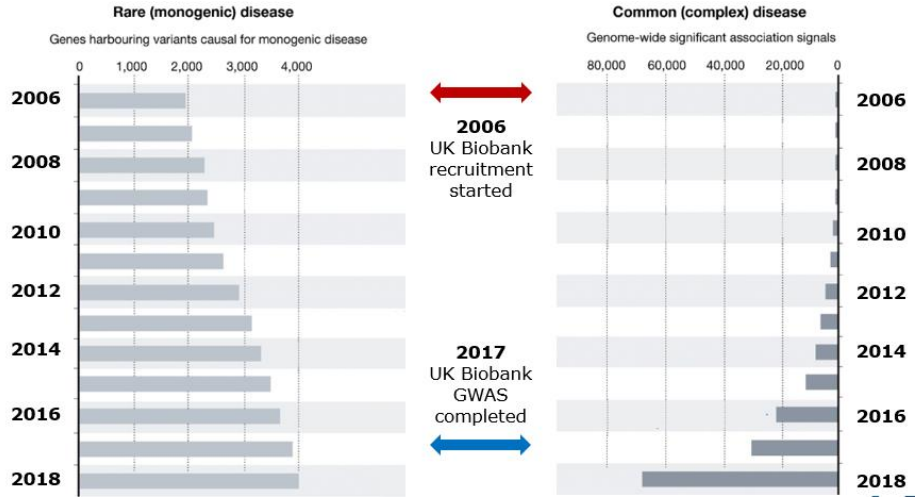
Wave's versatile RNA medicines platform ideal for capitalizing on new genetic insights in rare and common diseases

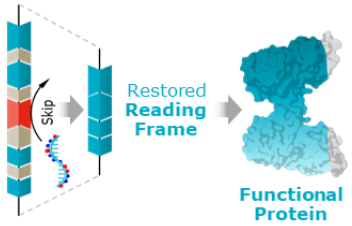


editing

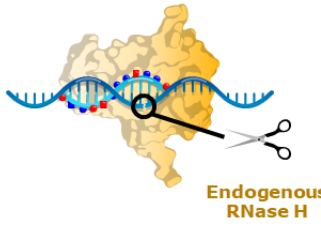


siRNA silencing





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

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

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

Program	Discovery	Preclinical	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 (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)

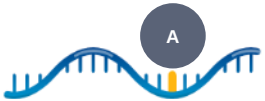
Editing for correction

Editing for upregulation

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

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)

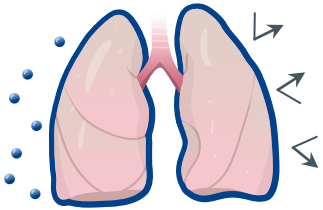
Edited *SERPINA1* mRNA enables wild-type M-AAT protein production

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

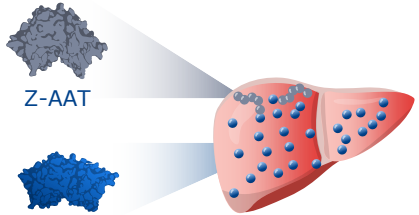
1) Restore circulating, functional wild-type M-AAT

2) Reduce Z-AAT protein aggregation in liver

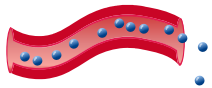
3) Retain M-AAT physiological regulation



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

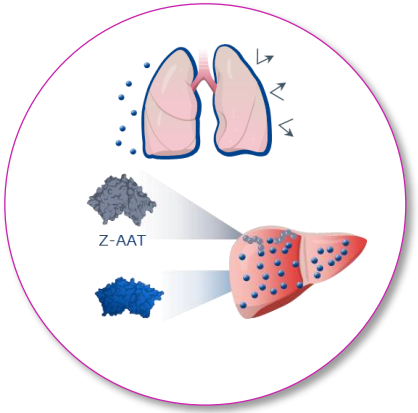
200,000 Pi*ZZ patients in US and Europe

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.

Data support WVE-006 as best-in-class approach for AATD

Preclinical *in vitro* and *in vivo* datasets demonstrate:

- ✓ **Significant increase in serum AAT of up to 30 uM in NSG-PiZ mice**
  - ~50% editing supports restoration to MZ phenotype
- ✓ **Restored wild-type M-AAT protein**
  - ~50% of AAT protein in serum is wild-type M-AAT
- ✓ **Editing is highly specific**
  - No bystander edits
- ✓ **Functionality of M-AAT protein**
  - >3-fold improvement in neutrophil elastase inhibition activity
- ✓ **Improvement in liver phenotype**
  - Decreased lobular inflammation and PAS-D globule size, prevents increase in hepatocyte turnover

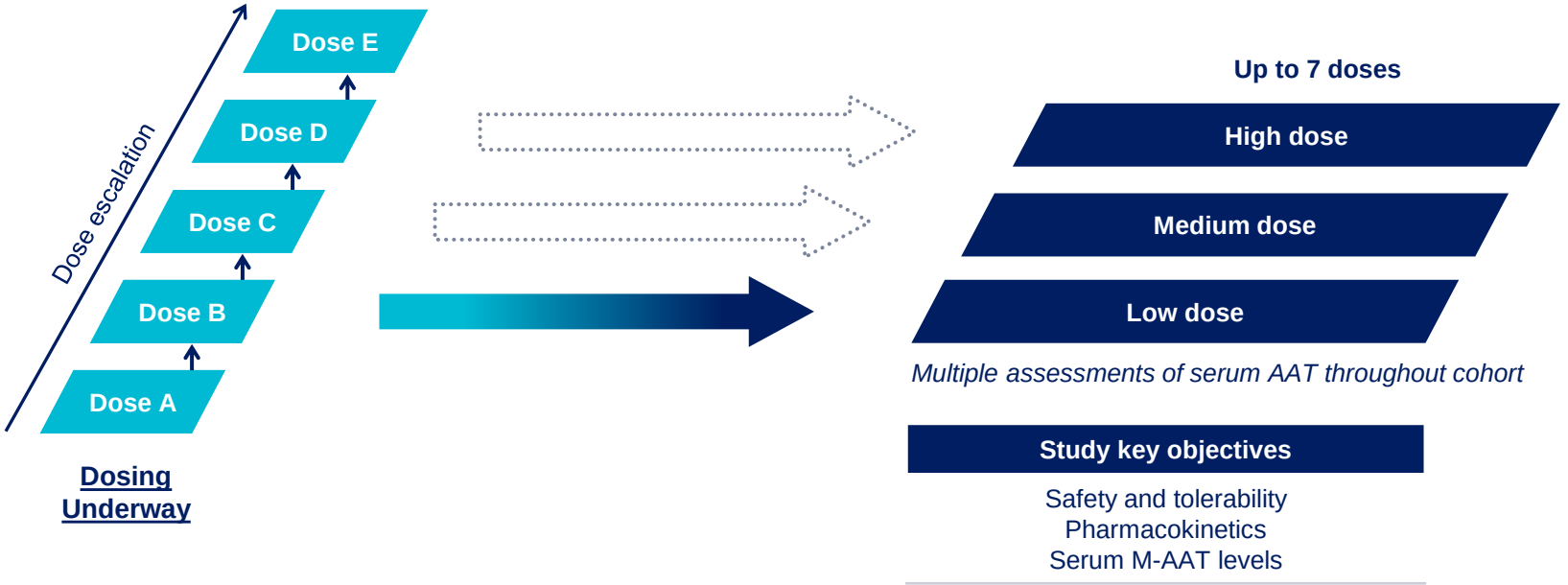


WVE-006 potential to address all key treatment goals with durable, subcutaneous delivery

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

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

SAD → MAD cohorts

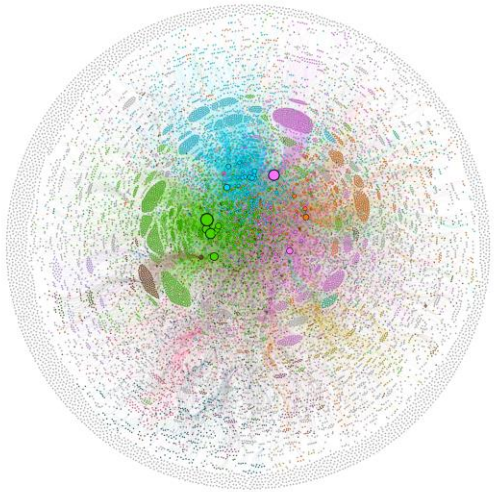


HV: healthy volunteer; SAD: single-ascending dose; MAD: multi-ascending dose

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



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

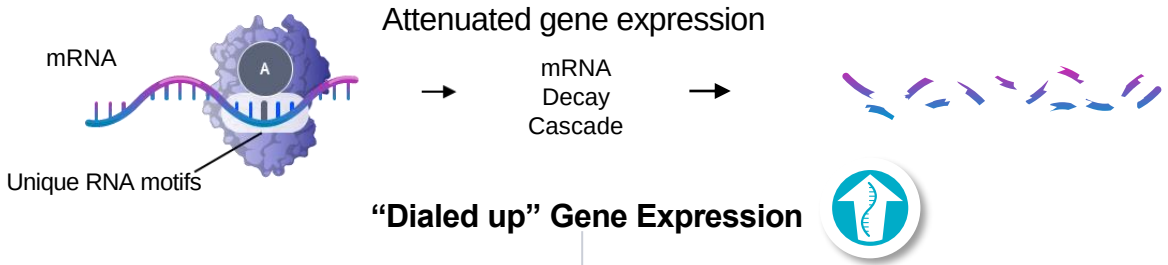
Innovating on applications of ADAR beyond restoring protein function

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

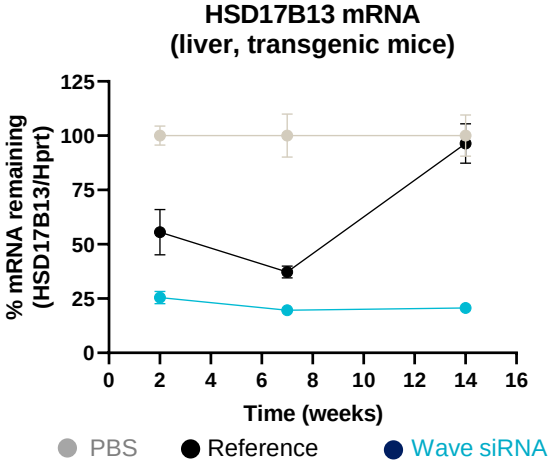
- The Edit-verse is substantial and still expanding
- Advancing work for a diverse set of undisclosed targets addressing areas of high unmet need, including both rare and prevalent diseases

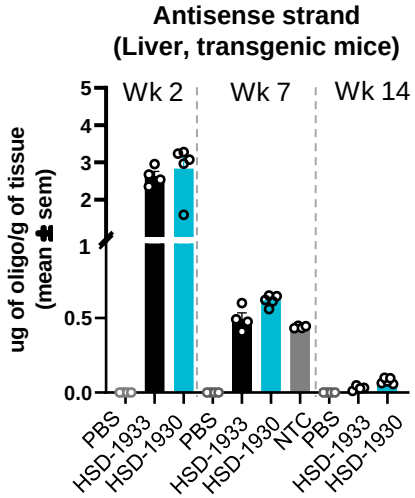
Potential for best-in-class siRNA enabled by Wave's PRISM platform

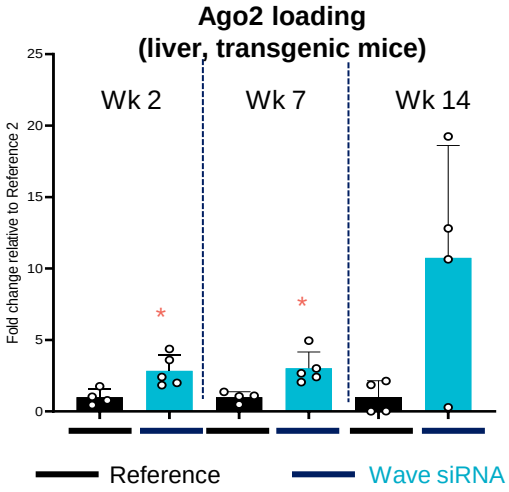
Nucleic Acids Research

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

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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 emerging from GSK collaboration

GLP-1 receptor agonists have several reported limitations

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

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]

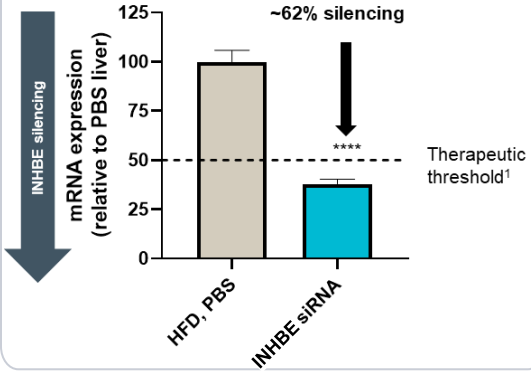
≥50% reduction of INHBE in patients expected to restore and maintain a healthy metabolic profile

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.

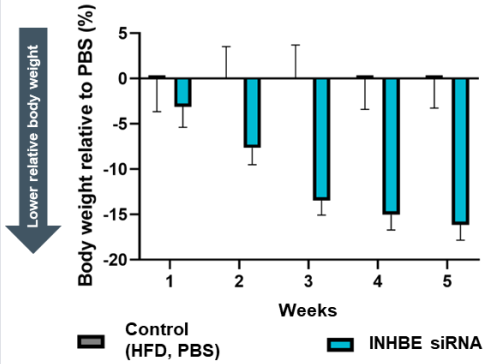
1. Nat Commun 2022. https://doi.org/10.1038/s41467-022-32398-7; 2. Nat Commun 2022. https://doi.org/10.1038/s41467-022-31757-8; 3. PLOS ONE 2018. https://doi.org/10.1371/journal.pone.0194798; 4. Adam, RC. et.al. Proc Natl Acad Sci USA. 2023, 120(32): e2309967120. 5. Yogosawa et al. 2013 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3526038/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

INHBE silencing achieved *in vivo* with GalNAc-siRNA led to lower body weight and significant decrease in visceral fat

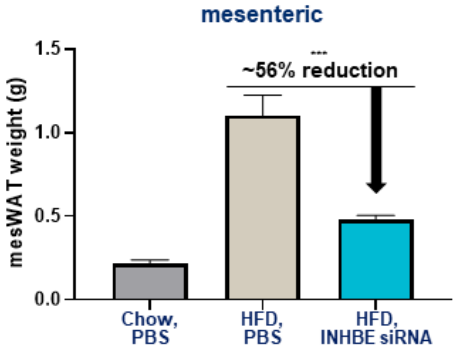
INHBE mRNA silencing demonstrated at 5 weeks



INHBE silencing led to 16% lower body weight as compared to control



INHBE silencing leads to significant decrease in visceral fat at 5 weeks

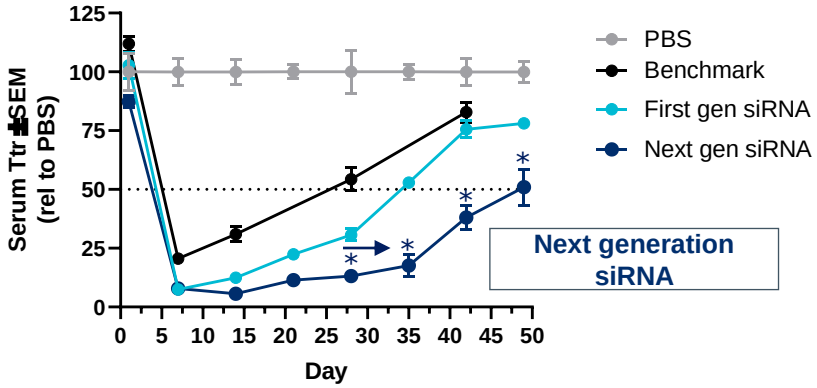


Results of *in vivo* preclinical study are consistent with UK Biobank human data on loss-of-function carriers

HFD: high-fat diet. Stats: two-sided Welch's T Test **** P < 0.0001 1. Adam, RC. et.al. Proc Natl Acad Sci USA. 2023. Data plotted by body weight difference as a % of PBS treated young DIO mice; Coskun, T. et. al. Mol. Metab. 2018, 18, 3. Stats: Repeated Measures ANOVA; Inhbe siRNA vs. Control sig. different at P < 0.05 level weeks 2 - 5; Stats: white-adj. Two-way ANOVA with Bonferroni-adj post hoc comparisons per tissue type allowing heteroscedasticity (only HFD, Inhbe siRNA vs. HFD, PBS shown) ***P < 0.001, ****P < 0.0001

INHBE candidate for obesity expected in 3Q 2024; CTA expected in 2025

Next generation siRNA results in more potent and durable target knockdown



Applying next-generation siRNA chemistry to INHBE program

- ✓ Potent and highly specific INHBE leads identified
- ✓ GalNAc-conjugated for targeted delivery to liver
- ✓ Potential for infrequent administration

Wave's next generation GalNAc-siRNA demonstrates best-in-class potential

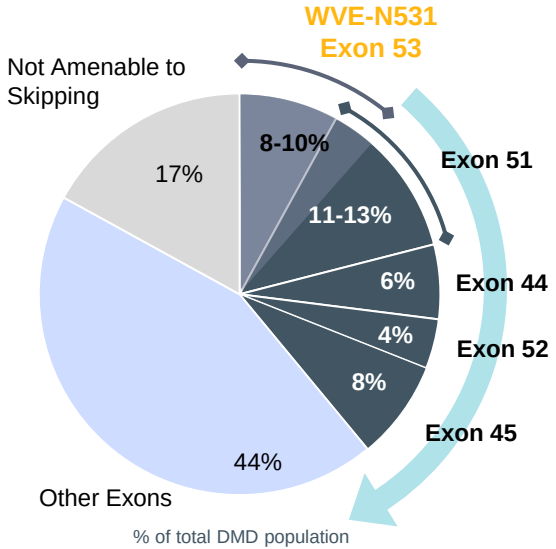
Foster, DJ. et.al. Mol Ther. 2018, 26(3), 708. B6 mice administered PBS or 0.5 mg/kg of siRNA (subcutaneous). Benchmark: Stats: Mixed Two-way ANOVA followed by post hoc test comparing siRNA vs. Next gen siRNA per day derived from linear mixed effects model * P < 0.0001

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

WVE-N531 may address high unmet need in DMD patients

- Increasing amount of **functional dystrophin** expression over minimal amount shown with approved therapies is expected to result in greater benefit for boys with DMD
- **Dystrophin protein established by FDA as surrogate endpoint** reasonably likely to predict benefit in boys[1]
- Differentiated profile with high muscle concentration
  - In NHPs, concentrations in heart and diaphragm were higher than skeletal muscles

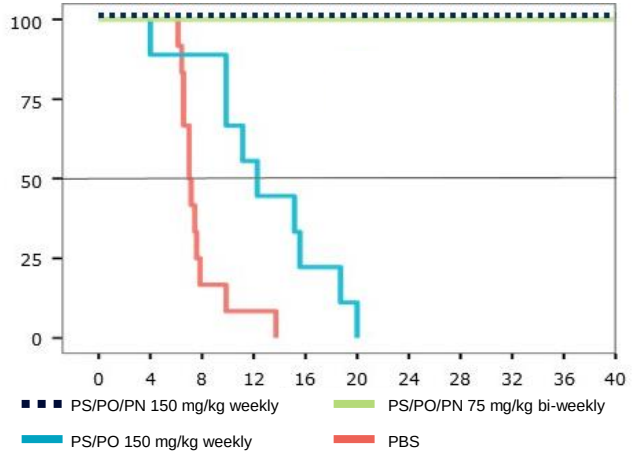
Potential to address up to 40% of DMD population



[1]. Vyondys: www.fda.gov; viltepso; www.fda.gov; Exondys; www.fda.gov; Amondys: www.fda.gov
Aartsma-Rus, et al. 2009 Hum Mutat 30, 293.

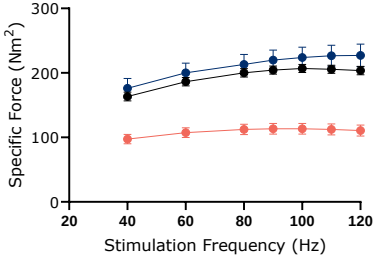
Extended survival in dKO preclinical model supports potential of Wave's PN-modified exon-skipping therapeutics for DMD

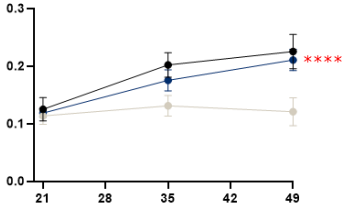
100% survival at time of study termination

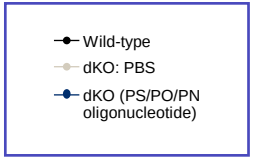


Note: Untreated, age-matched mdx mice had 100% survival at study termination [not shown]

Restored muscle and respiratory function to wild-type levels







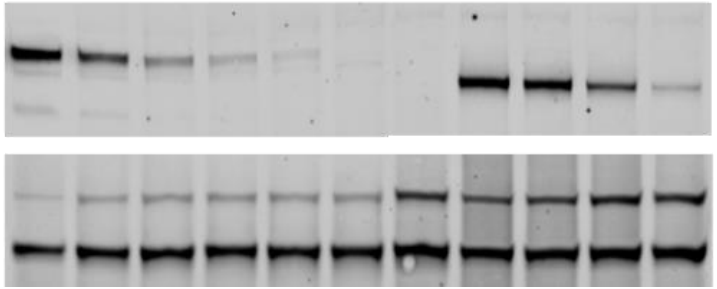
PN chemistry improved function and survival in dKO mice

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

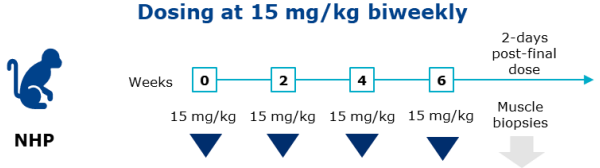
Preclinical data supported advancing WVE-N531 to clinical development

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

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



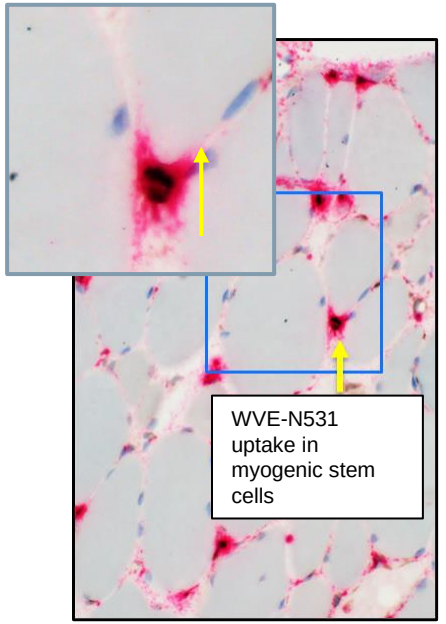
	Mean Tissue Concentration		
	Skeletal muscle	Diaphragm	Heart
15 mg/kg* IV dose	2.17 ug/g	10.8 ug/g	57.2 ug/g

*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	**42 µg/g**
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**

WVE-N531 uptake in myocyte stem cells



Important for potential muscle regeneration

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) 42 µg/g = 6.1 µM; 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 and dosing underway

FORWARD-53

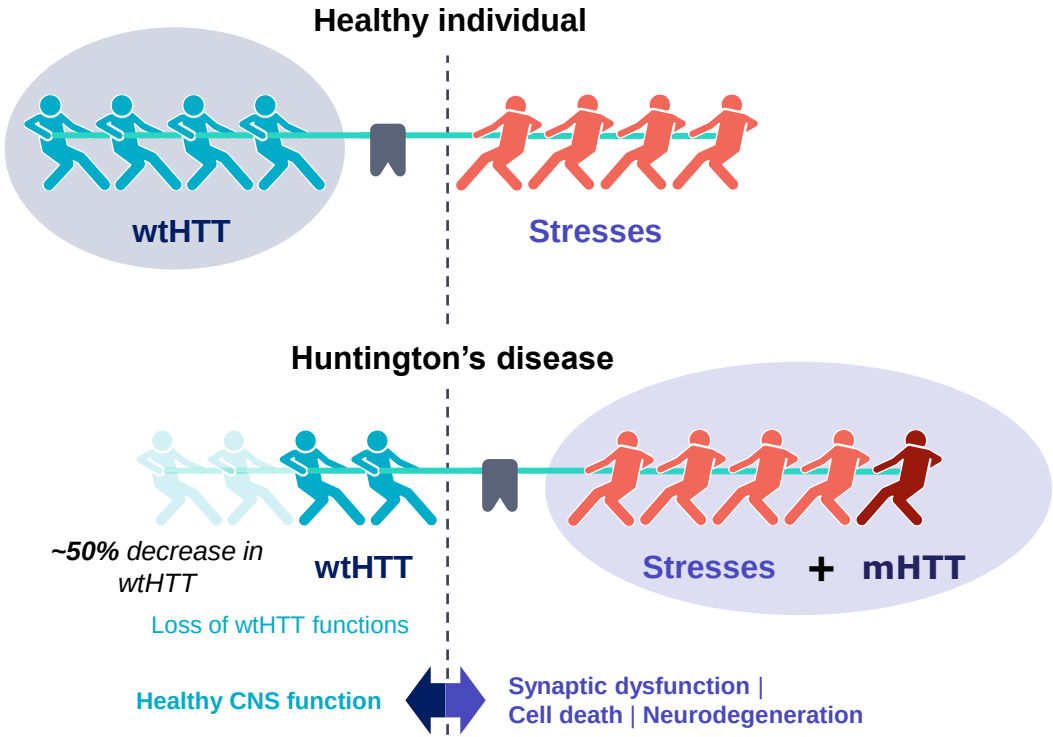
Potentially registrational 24-week dystrophin expression data are expected in 3Q 2024

IV: intravenous; NSAA: North star ambulatory assessment

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



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

Selective, potent, and durable reduction of mHTT in preclinical models

- ✓ Allele-selectivity demonstrated *in vitro*
- ✓ Durable mHTT knockdown demonstrated for 12 weeks in BACHD mouse model
- ✓ NHP study demonstrated significant tissue exposure levels of WVE-003 in deep brain regions

Target engagement demonstrated with single doses in clinic

- ✓ Reduction in mean CSF mHTT and preservation of wtHTT observed in pooled analysis of single-dose cohorts:
  - 35% reduction in mHTT versus placebo
  - 22% reduction in mHTT from baseline

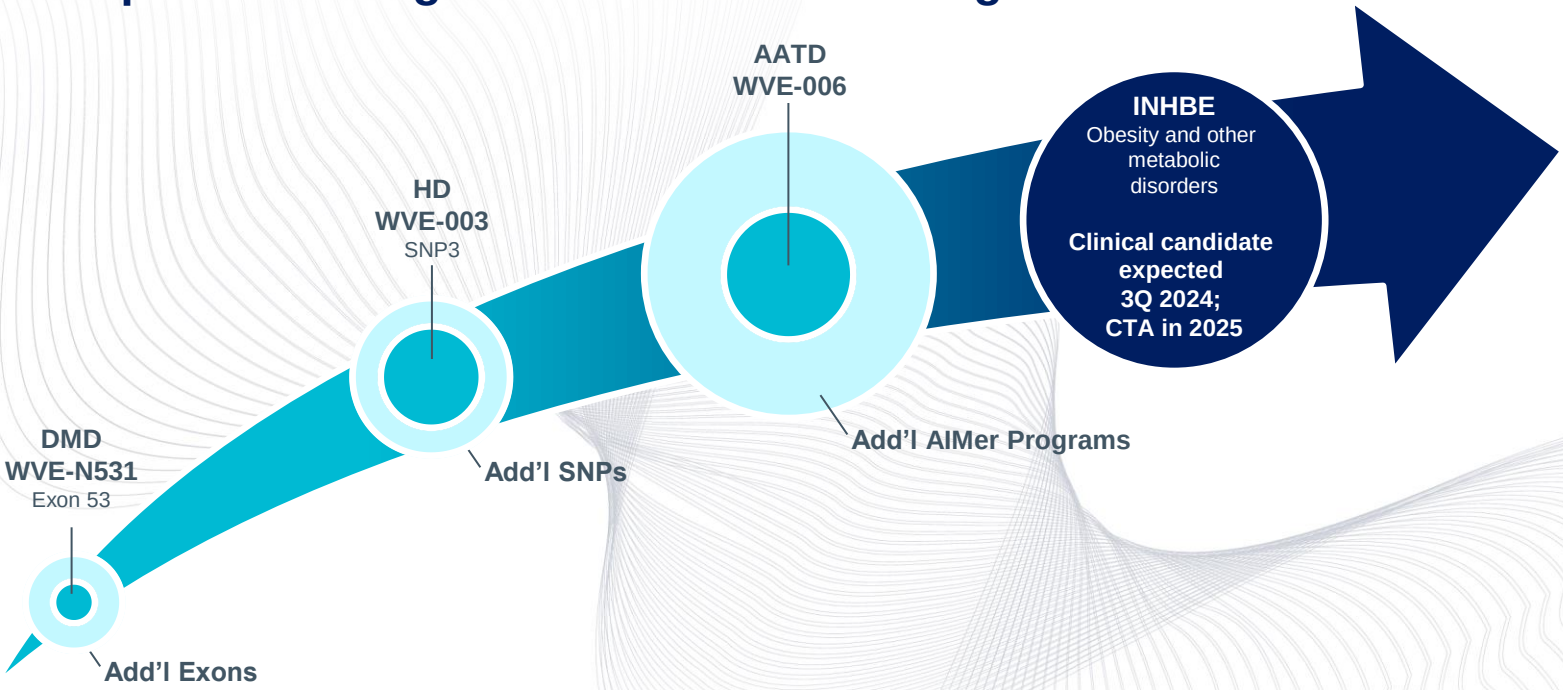
Advancing multi-dose cohort in SELECT-HD Phase 1b/2a clinical trial

- WVE-003 currently being evaluated in 30mg Q8W multi-dose cohort
- Multi-dose data expected to enable decision making on program and support opt-in package to Takeda

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

Wave is poised for significant and sustained growth



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

Note: Bubble size illustrative of size of total addressable US market (assuming 100% share of addressable patients); M: million
* In US and Europe

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 Program (Obesity) *Driven by clinical genetics, with potential to be next-generation therapeutic for obesity*	**3Q 2024:** Select INHBE clinical candidate **2025:** Submit a clinical trial application (CTA)
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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