Wave Life Sciences

Second Quarter 2022 Earnings

August 11, 2022

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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.

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Paul Bolno, MD, MBA

President and CEO

Today's agenda

1. **Recent business highlights -** Paul Bolno, MD, MBA, President and CEO
2. **Advancing a differentiated therapeutic pipeline -** Michael Panzara, MD, MPH, CMO, Head of Therapeutics Discovery and Development
3. **Expanding Wave's RNA base editing applications –** Chandra Vargeese, PhD, CTO, Head of Platform Discovery Sciences
4. **2Q 2022 financial results –** Kyle Moran, CFA, CFO
5. **Closing remarks –** Paul Bolno, MD, MBA, President and CEO
6. **Q&A**

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Second quarter 2022 and recent highlights

Rapidly advancing first-in-class RNA editing modality to clinic

- WVE-006 selected as AATD development candidate; CTA submissions expected in 2023
- First-in-class RNA editing candidate and most advanced program currently in development using an oligonucleotide to harness an endogenous enzyme for editing

Progressing differentiated next-generation clinical pipeline

- Preclinical data continues to translate into differentiated pharmacology in DMD and HD studies
- Multiple clinical data readouts on track to be announced in 2H 2022

Well-capitalized to execute on several upcoming milestones

- Completed $70 million underwritten offering in June 2022
- Executing on multiple pillars to drive shareholder value

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

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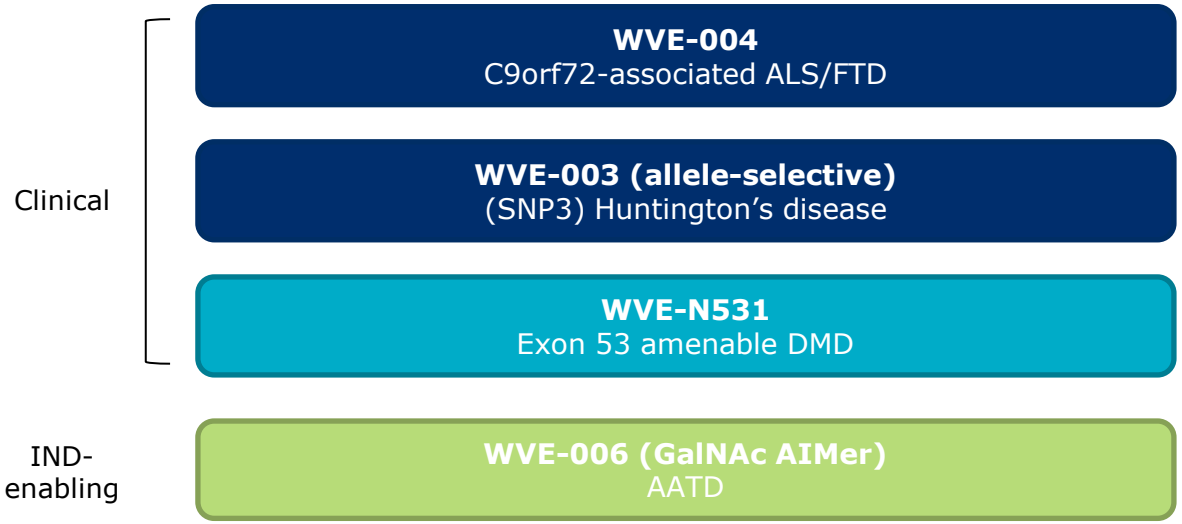
Mike Panzara, MD, MPH

Chief Medical Officer,

Head of Therapeutics

Discovery and Development

Advancing an innovative and differentiated therapeutic pipeline



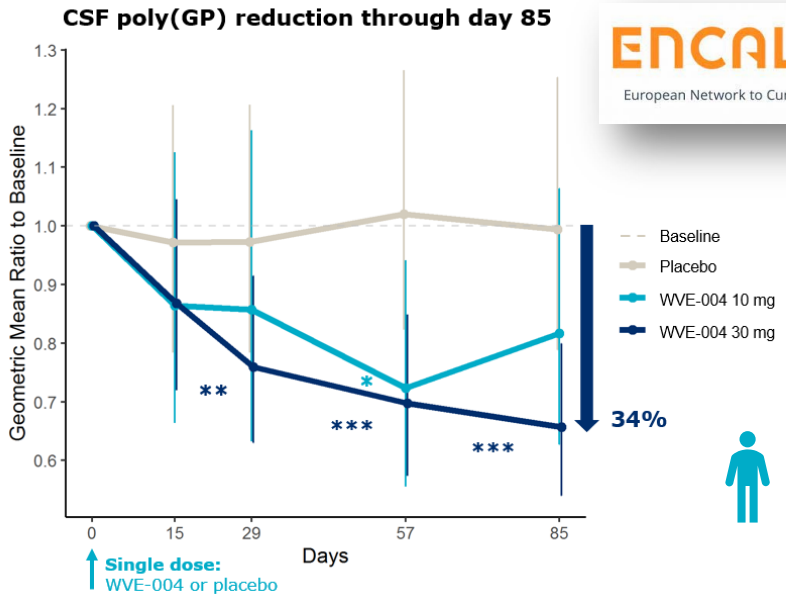
WVE-004 FOCUS-C9 clinical trial (NCT04931862); WVE-003 SELECT-HD clinical trial (NCT05032196); WVE-N531 open-label clinical trial (NCT04906460); AIMer: RNA editing oligonucleotide

WVE-004 clinical data demonstrate successful translation of preclinical approach to clinic

PK/PD modeling using preclinical *in vivo* models predicted pharmacodynamically active starting dose

- ✓ Poly(GP) reduction in cortex and spinal cord in transgenic mice with WVE-004
- ✓ Sufficient concentrations of WVE-004 in cortex and spinal cord of NHP for target engagement

Target engagement confirmed in patients supports advancing FOCUS-C9 clinical study



Additional single and multidose clinical data expected in 2H 2022

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 presented at ENCALS Meeting (June 1-3, 2022)

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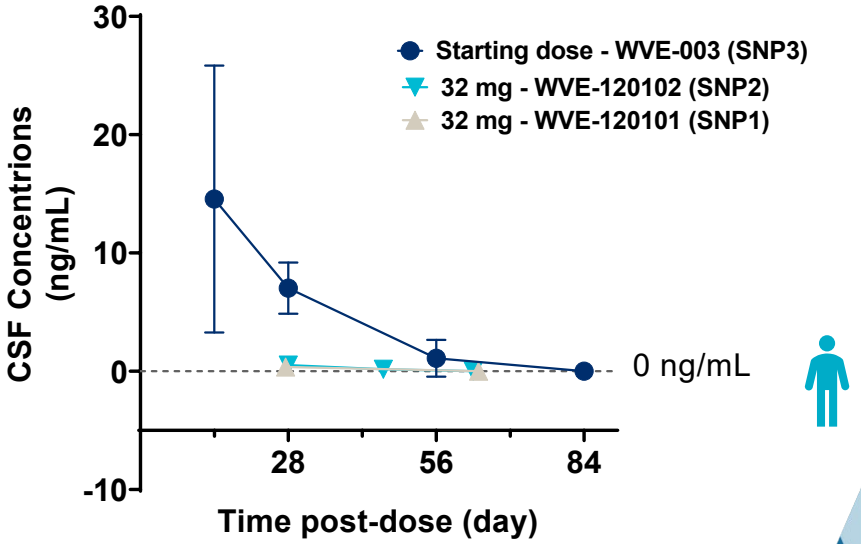
WVE-003 (allele-selective compound in HD) achieves concentrations in patient CSF expected to engage target

PK/PD modeling using preclinical *in vivo* models predicted pharmacodynamically active starting dose

- ✓ Demonstrated allele selectivity for mHTT
- ✓ mHTT reduction in cortex and striatum in transgenic mice with WVE-003
- ✓ Achieved sufficient concentrations of WVE-003 in NHP brain tissues for target engagement

Blinded CSF WVE-003 concentrations compared to CSF WVE-120102/WVE-120101 concentrations



Dose escalation continues in ongoing SELECT-HD clinical trial
Clinical data expected in 2H 2022

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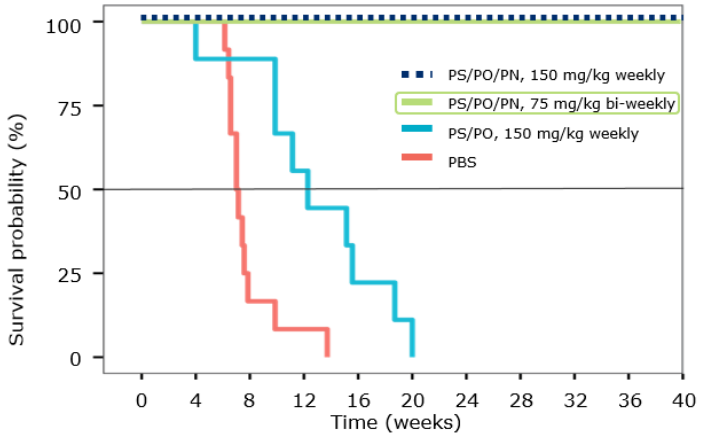
WVE-120101 (SNP1) and WVE-120102 (SNP2): First-generation PS/PO compounds for HD

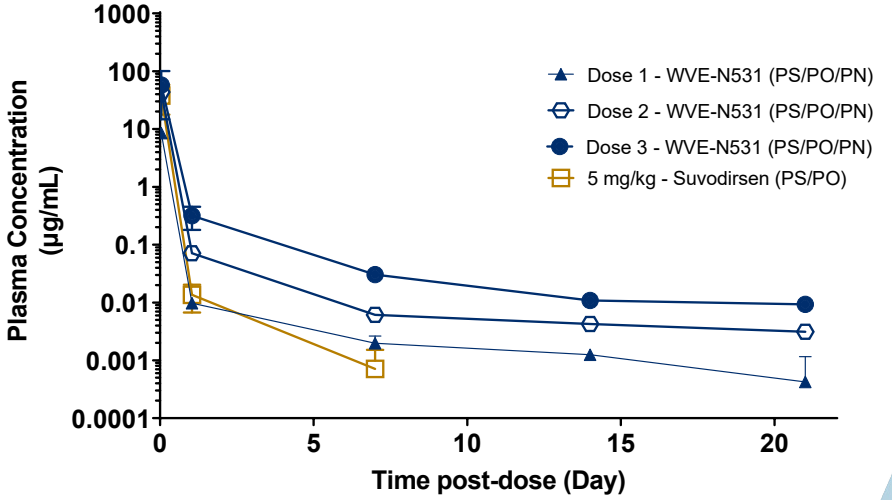
Currently dosing at human equivalent doses in the range explored in preclinical dKO model

dKO mouse model

- ✓ Treatment with PN-modified molecules led to 100% survival of dKO mice at time of study termination



Plasma WVE-N531 concentrations compared to plasma suvodirsen concentrations



Dosing underway at Dose 4 of WVE-N531
Clinical data, including muscle biopsies, expected in 4Q 2022

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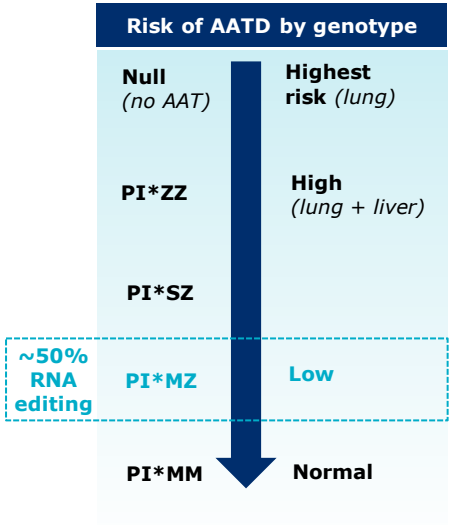
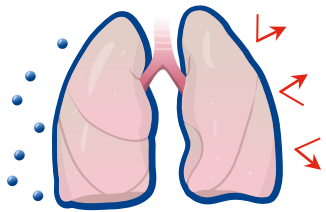
WVE-006: designed to correct mutant AATD transcript to address both liver and lung manifestations of AATD

AATD is an inherited genetic disorder that is commonly caused by a G-to-A point mutation ("Z allele") in the *SERPINA1* gene, which leads to lung disease due to lack of wild-type alpha1-antitrypsin (M-AAT) in lungs and liver disease due to aggregation of misfolded Z-AAT protein in hepatocytes



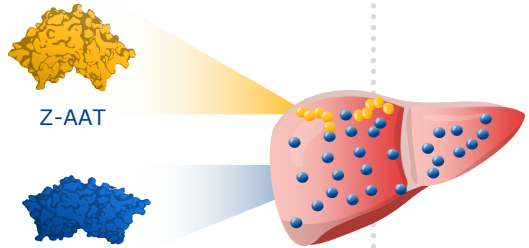
WVE-006 ADAR editing approach to address key goals of AATD treatment:

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



M-AAT reaches lungs to protect from proteases

2) Reduce Z-AAT protein aggregation in liver



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

3) Retain M-AAT physiological regulation

M-AAT secretion into bloodstream

~200K people in US and EU with mutation in *SERPINA1* Z allele (PI*ZZ)

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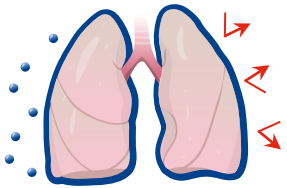
AAT: Alpha-1 antitrypsin Strnad *et al*., 2020 *N Engl J Med* 382:1443-55; Blanco *et al*., 2017 *Int J Chron Obstruct Pulmon Dis* 12:561-69; Remih *et al.*, 2021 *Curr Opin Pharmacol* 59:149-56.

AATD AIMer restores functional M-AAT protein and alleviates liver aggregates in preclinical model

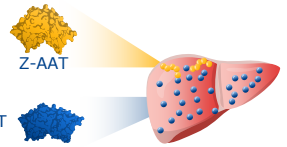
Correction of loss-of-function phenotypes

Restored M-AAT reaches lungs to protect from proteases



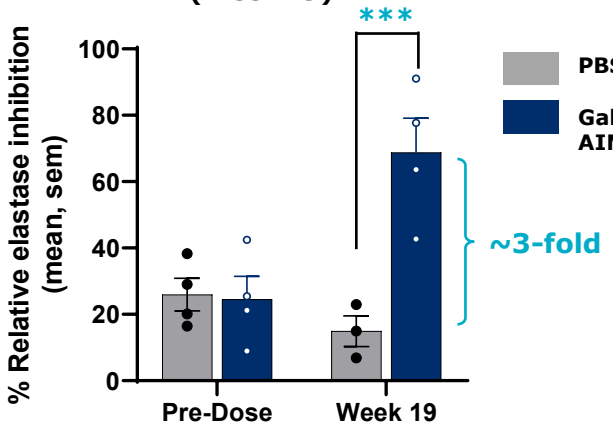
HYBRID EVENT TIDES USA | Oligonucleotide & Peptide Therapeutics

Correction of gain-of-function phenotypes

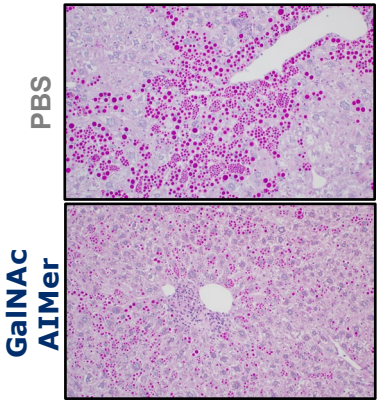


Wild-type M-AAT protein replaces Z-AAT with RNA correction

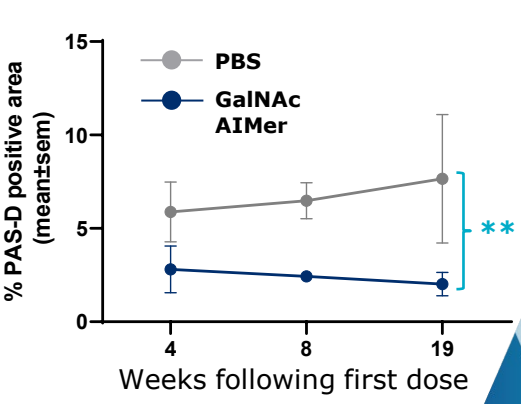
Neutrophil elastase inhibition (Week 19)



PAS-D staining (19 weeks)



PAS-D-positive area declines with AIMer treatment



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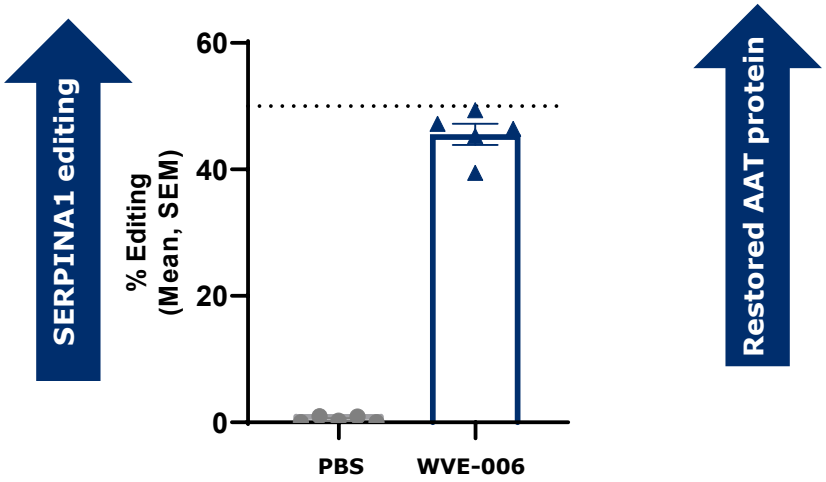
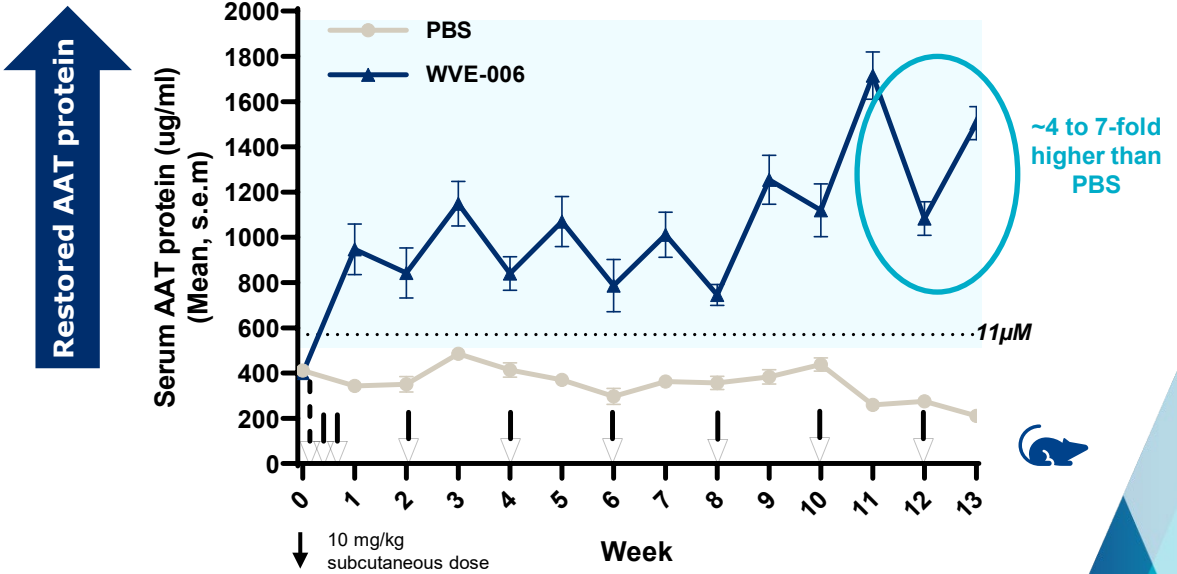
GalNAc AIMer (SA1-5) administered bi-weekly (10 mg/kg) following initial loading dose (3 x 10 mg/kg) in hu*ADAR/SERPINA1* mice (8–10 weeks old); Left: Neutrophil elastase inhibition assay (pre-dose, week 19 serum samples), Stats: Mixed effects analysis P<0.001; Right: 20x images from liver stained with PAS-D at 19 weeks ** p<0.01

WVE-006 results in circulating AAT protein levels well above established 11μM threshold in vivo

SERPINA1 mRNA editing in liver of AATD mouse model (NSG-PiZ mice) (Week 13)



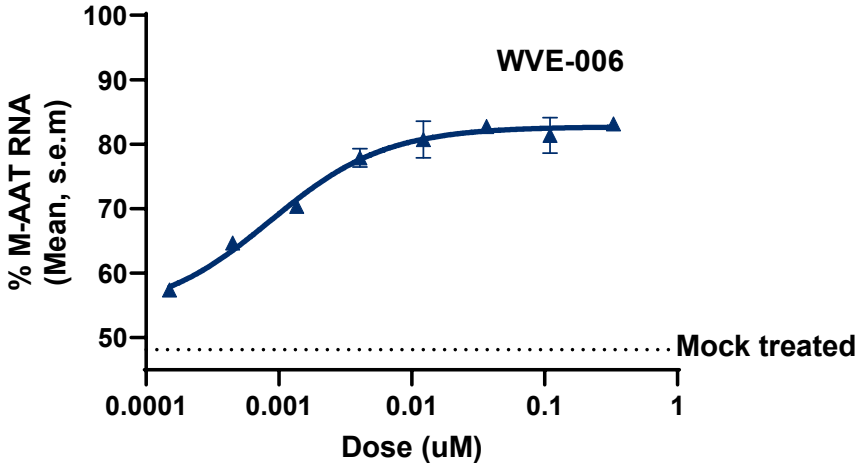
WVE-006 treatment results in serum AAT protein levels >11 uM in AATD mouse model (NSG-PiZ mice)



WVE-006 is a GalNAc-conjugated AIMer (A to I(G) RNA base editing oligonucleotide); WVE-006 administered in 7-week old NSG-PiZ mice (n=5 per group); Left: Liver biopsies collected at week 13 (one week after last dose) and SERPINA1 editing was quantified by Sanger sequencing; Stats: One-way ANOVA with adjustment for multiple comparisons (Tukey); Right: Total serum AAT protein quantified by ELISA; Stats: Two-Way ANOVA with adjustment for multiple comparisons (Tukey)

WVE-006 results in efficient editing in primary human hepatocytes, further supporting strong candidate profile

Efficient SERPINA1 editing in donor-derived primary human hepatocytes with WVE-006 (MZ genotype)



Note: Due to MZ genotype, Y-axis ranges from ~50-100%

- ✓ Efficient SERPINA1 and circulating AAT protein restoration *in vivo* demonstrated in AATD mouse model
- ✓ Concentration-dependent RNA editing *in vitro* demonstrated in primary human hepatocytes (MZ genotype)
- ✓ IND-enabling activities underway

CTA submissions for WVE-006 expected in 2023

Primary human hepatocytes from an MZ donor treated with WVE-006 (GalNAc AIMer) at indicated doses for 48 hrs; SERPINA1 editing was quantified by Sanger sequencing

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Chandra Vargeese, PhD

Chief Technology Officer,

Head of Platform

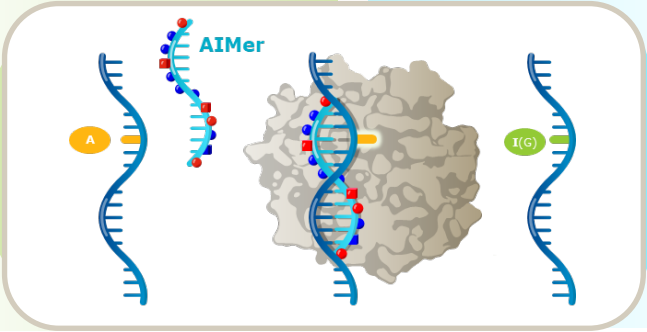
Discovery Sciences

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**
✓ **Upregulate expression**

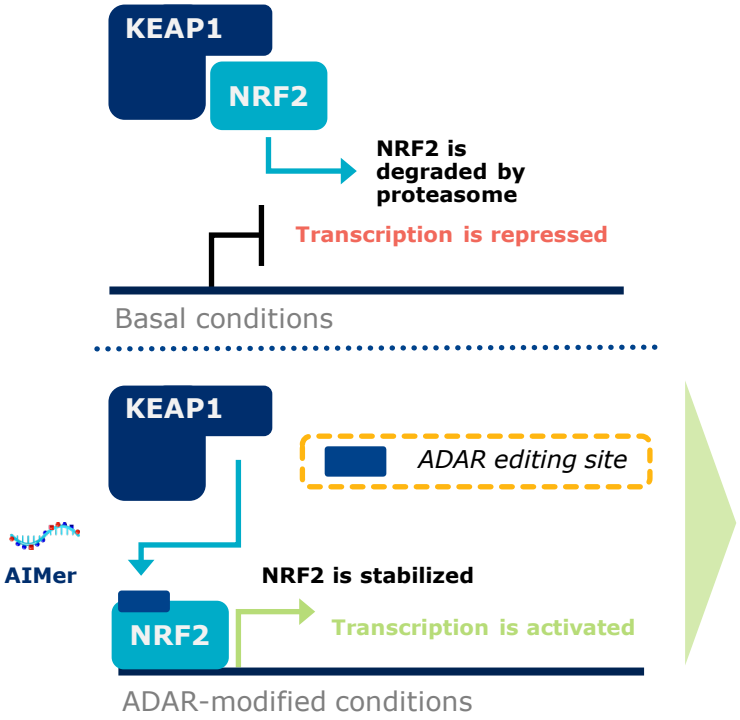
Achieved POC

- Modify function
- Post-translational modification
- Alter folding or processing

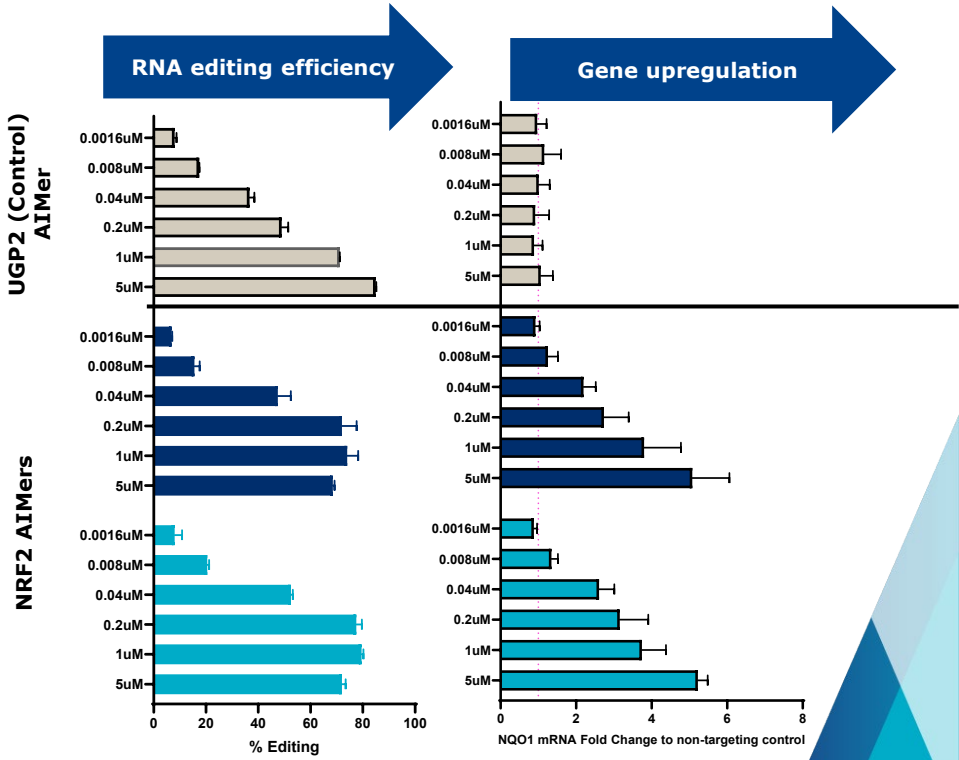
Potential to precisely control gene upregulation with a titratable therapeutic approach

POC: proof of concept

Dose dependent modulation of protein/protein interactions

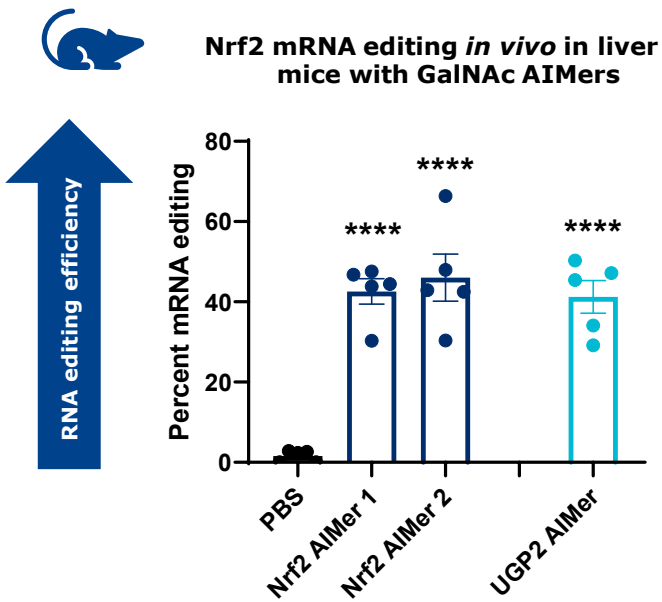


Dose-dependent gene upregulation (NQO1) *in vitro* following Nrf2 editing to disrupt protein/protein interaction

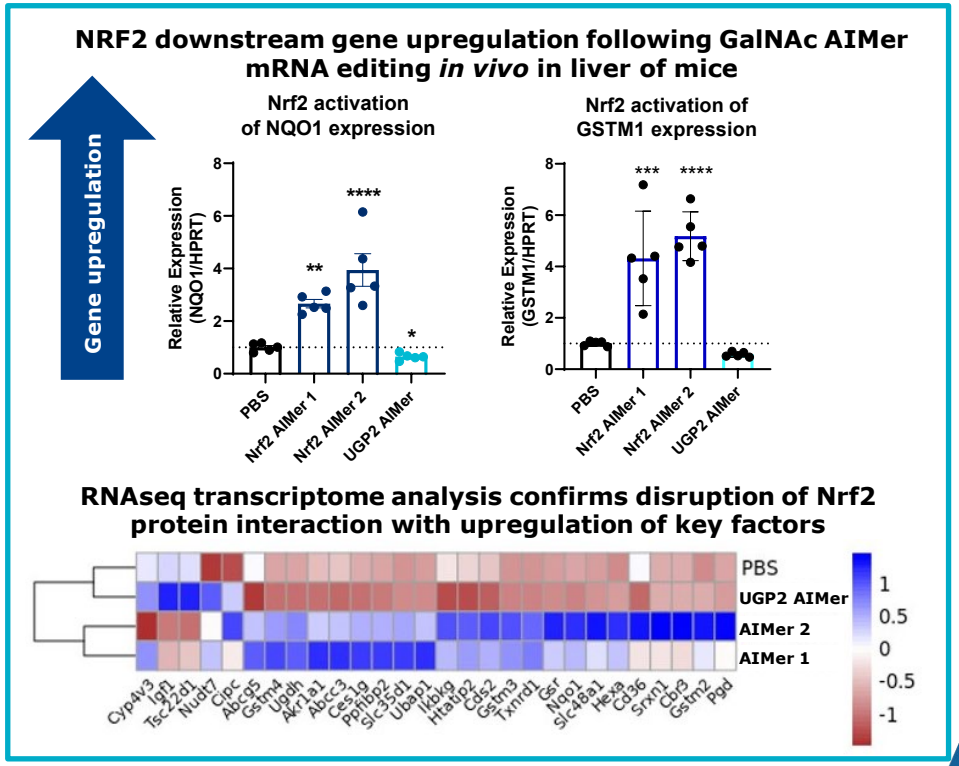


n=2; Primary hepatocytes 48h of treatment with the indicated dose concentration of AIMers

AIMers enable activation of gene pathway *in vivo* with single edit



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



Methods: hADAR C57BL/6 mice dosed subQ (days 0, 2, 4) at 10mg/kg GalNAc-conjugated AIMers. Livers harvested (day 7), analyzed for editing and NQO1 expression via Sanger sequencing or qPCR, respectively. Data analyzed via One-way ANOVA with Tukey's multiple comparison test. Asterisks indicate statistical significance to PBS-treated animals as follows: * = p<0.05; ** = p<0.01; *** = p<0.001; **** = p<0.0001

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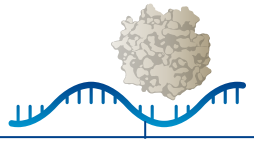
Upregulation: AIMers can edit RNA motifs to restore or upregulate gene expression

RNA binding proteins recognize sequence motifs to regulate various mRNA properties



mRNA

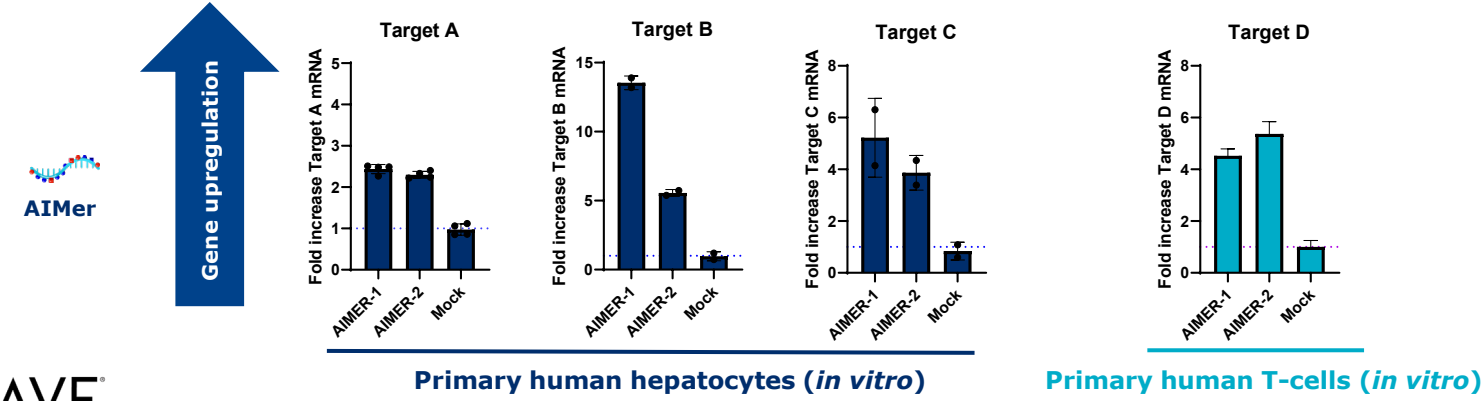
Processing
- Splicing
- PolyA usage
- Capping

Transport
- Intracellular localization

Stability
- Inhibit or enhance mRNA decay

Protein production
- Translational efficiency

Editing RNA Motifs to regulate RNA half-life to upregulate RNA expression is possible for clinically-relevant targets, including both metabolic and immune targets



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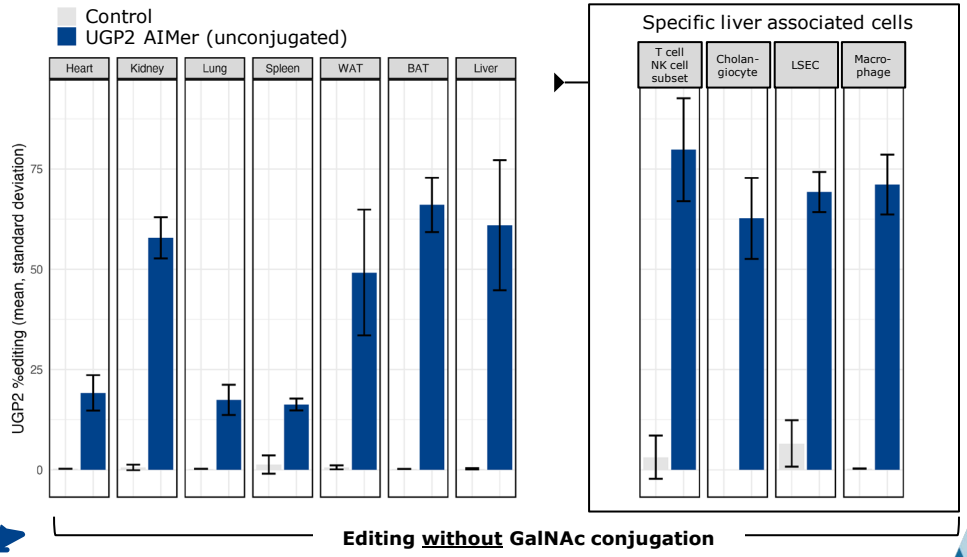
Systemic *in vivo* editing without delivery vehicles

Editing: Potent, durable, specific A → I (G) RNA editing

Delivery: Efficient RNA editing in preclinical *in vivo* models:

- ✓ Targeted delivery (GalNAc)
- ✓ Systemic delivery
- ✓ Local delivery (IT, IVT, others)

Substantial RNA editing across multiple tissues following single subcutaneous dose of UGP2 AIMer



Potential to accelerate timelines to candidate with AIMer pipeline expansion

Right: Single dose of 100mg/kg unconjugated UGP2 AIMer, seven days post dose; WAT: White adipose tissue; BAT: Brown adipose tissue; CD3+: T-cells and subset of NK cells; EpCAM+(Epithelial cell adhesion molecule): mainly cholangiocytes within liver; LSEC cells (Liver Sinusoidal Endothelial Cells); M0 cells: macrophages

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Kyle Moran, CFA

Chief Financial Officer

Second quarter 2022 financial results

	Three Months Ended June 30, 2022	Three Months Ended June 30, 2021
Figures are in thousands, except per share amounts		
Revenue	$375	$2,776
Operating Expenses:		
Research and Development	29,733	31,635
General and Administrative	12,806	10,969
Total Operating Expenses	42,539	42,604
Net Loss from Operations	(42,164)	(39,828)
Total Other Income, Net	868	1,062
Income Tax Provision, net	--	--
Net Loss	($41,296)	($38,766)
Net Loss per Share	**($0.62)**	**($0.78)**

As of June 30, 2022	**Ordinary Shares:** 86.7 million	**Cash, Cash Equivalents & Short-Term Investments:** $148.2 million

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Wave expects that its existing cash, cash equivalents and short-term investments will enable the company to fund its operating and capital expenditure requirements to the end of 2023.

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Paul Bolno, MD, MBA

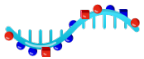
President and CEO

Wave Life Sciences is well-positioned to become a leading genetic medicines company

Innovative oligonucleotide platform

- PN chemistry and preclinical modeling translating in clinic
- Potential for potent and durable therapeutics

Multiple therapeutic modalities



- Antisense
- Exon skipping
- RNA editing
- siRNA

Foundation to support pipeline growth

- Leveraging large and growing publicly available genetic datasets
- Discovery through clinical-stage capabilities
- GMP manufacturing

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Differentiated RNA therapeutics pipeline with multiple clinical datasets expected in 2H 2022

WVE-004 C9orf72 ALS & FTD	✓ Delivered clinical target engagement data with single doses • Additional single and multidose data in 2H 2022 • Discussions with regulatory authorities regarding next phase of development later in 2022 • Initiate an OLE clinical trial in 2H 2022	**Silencing**	**CNS** *(Intrathecal)*
WVE-003 HD SNP3	• Clinical data to enable decision making in 2H 2022		
WVE-N531 DMD Exon 53	• Clinical data to enable decision making in 4Q 2022	**Splicing**	**Muscle** *(IV)*
WVE-006 AATD	✓ Selected an AATD AIMer development candidate and initiated IND-enabling activities • Submit clinical trial applications in 2023	**ADAR editing**	**Targeted delivery liver** *(Subcutaneous)*

Additional data generated in 2022 expected to further inform future opportunities and unlock value

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WVE-004 FOCUS-C9 clinical trial (NCT04931862); WVE-003 SELECT-HD clinical trial (NCT05032196); WVE-N531 open-label clinical trial (NCT04906460)

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Q&A

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Realizing a brighter future for people affected by genetic diseases

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