Wave Life Sciences

First Quarter 2022 Earnings

May 12, 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. **Opening remarks -** Paul Bolno, MD, MBA, President and CEO
2. **Clinical pipeline -** Michael Panzara, MD, MPH, CMO, Head Therapeutics Disc. and Dev.
3. **1Q 2022 financial results –** Kyle Moran, CFO
4. **Closing remarks –** Paul Bolno, MD, MBA, President and CEO
5. **Q&A**

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First quarter 2022 and recent highlights

Multiple pillars to drive value

Clinical programs: WVE-004 clinical data suggests PN chemistry is translating in clinic

FOCUS C9

SELECT HD

WVE-N531 (DMD)

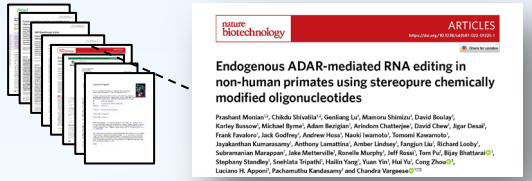
AATD program: Preclinical data highlighted at scientific meetings

OPT Congress 7th ANNUAL Oligonucleotide & Precision Therapeutics IN-PERSON ■ VIRTUAL FLEXIBLE REGISTRATION

HYBRID EVENT TIDES USA | Oligonucleotide & Peptide Therapeutics

ASGCT 25TH ANNUAL MEETING MAY 16-19 2022 WASHINGTON DC

Platform: Multiple publications across modalities GMP manufacturing



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

Liu et al. Molecular Therapy Nucleic Acids, 2022; doi: 10.1016/j.omtn.2022.04.007; Kandasamy et al. Nucleic Acids Research, 2022; doi: 10.1093/nar/gkac037; Monian *et al.*, 2022 *Nature Biotech* published online Mar 7, 2022 doi: 10.1038.s41587-022-01225-1

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Wave's AIMers have potential to uniquely address wide array of genetically-defined diseases

PRISM

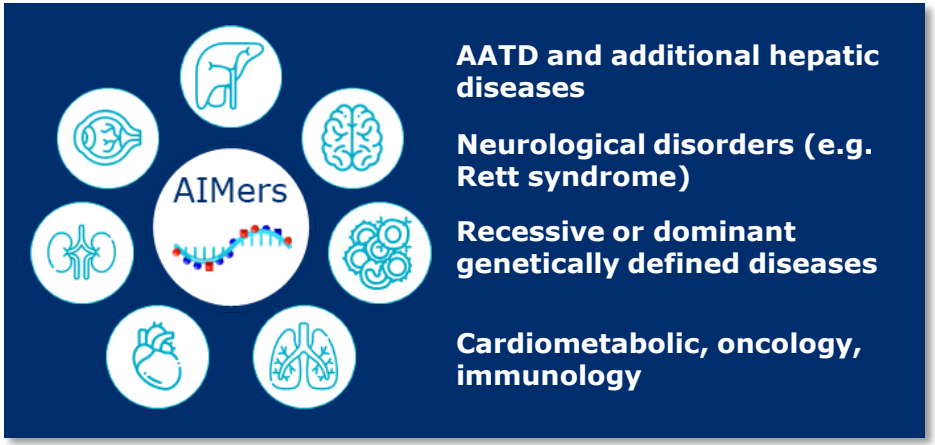
Editing: Potent, durable, specific A → I (G) RNA editing

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

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

AIMer opportunity

- **Correct** tens of thousands of pathogenic human SNPs potentially amenable to ADAR editing correction[1]
- **Modulate** protein interactions, e.g. **upregulation** of protein expression and **disruption** of protein-protein interactions



Potential to accelerate timelines to candidate with AIMer pipeline expansion

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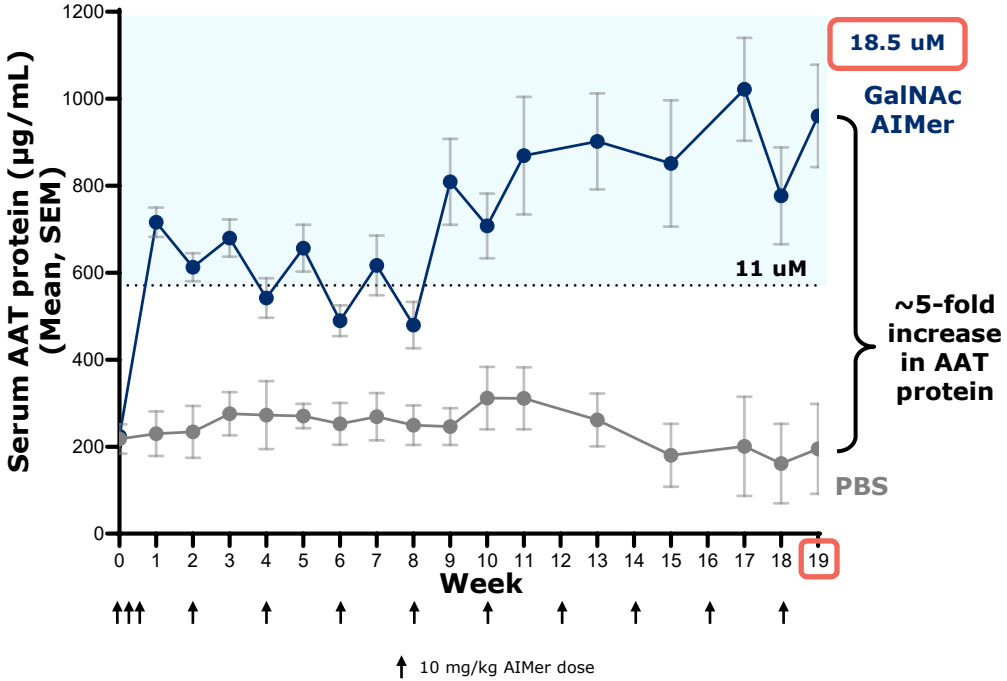
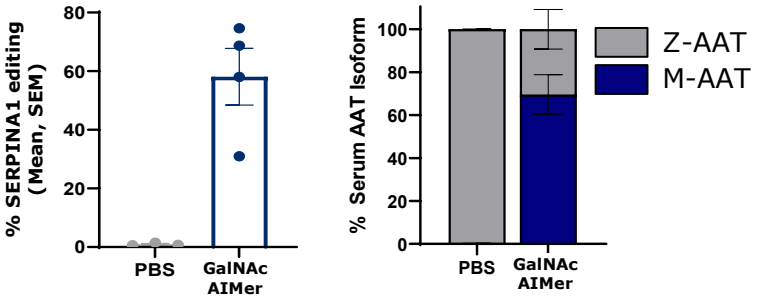
Monian *et al.,* 2022 *Nature Biotech* published online Mar 7, 2022 doi: 10.1038.s41587-022-01225-1; SNP: single nucleotide polymorphism
A: Adenosine; I: Inosine; G: Guanosine; AATD: alpha-1 antitrypsin disease; [1]ClinVar database

ADAR editing approach to restore healthy, wild-type AAT protein to address AATD with GalNAc-AIMers

GalNAc-AIMer results in serum AAT protein levels >11 uM at week 19



~60% RNA editing & ~70% serum M-AAT protein in mice (week 19 data)



HYBRID EVENT
TIDES USA | Oligonucleotide & Peptide Therapeutics

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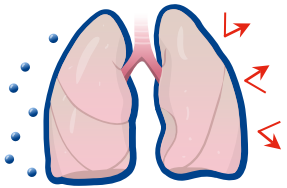
GalNAc AIMer (SA1-5) administered in hu*ADAR/SERPINA1* mice (8–10 weeks old) Left: Total serum AAT protein quantified by ELISA. Right: Liver biopsies collected at week 19 (one week after last dose); SERPINA1 editing was quantified by Sanger sequencing; Proportion of AAT protein in serum measured by mass spec, total AAT protein quantified by ELISA

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

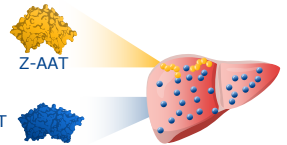
Correction of loss-of-function phenotypes

Restored M-AAT reaches lungs to protect from proteases



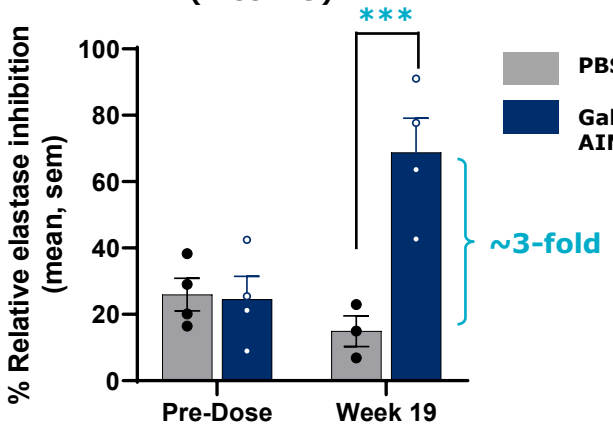
HYBRID EVENT TIDES USA | Oligonucleotide & Peptide Therapeutics

Correction of gain-of-function phenotypes

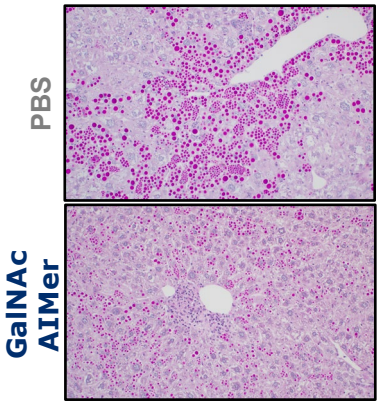


Wild-type M-AAT protein replaces Z-AAT with RNA correction

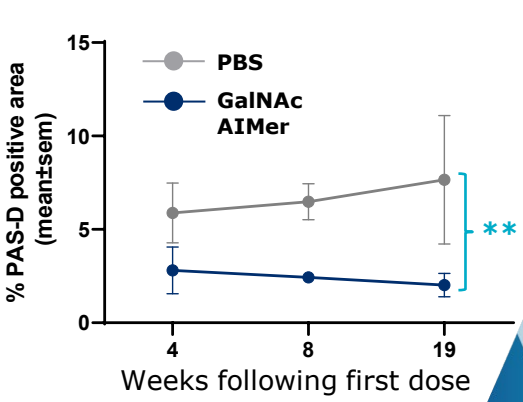
Neutrophil elastase inhibition (Week 19)



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

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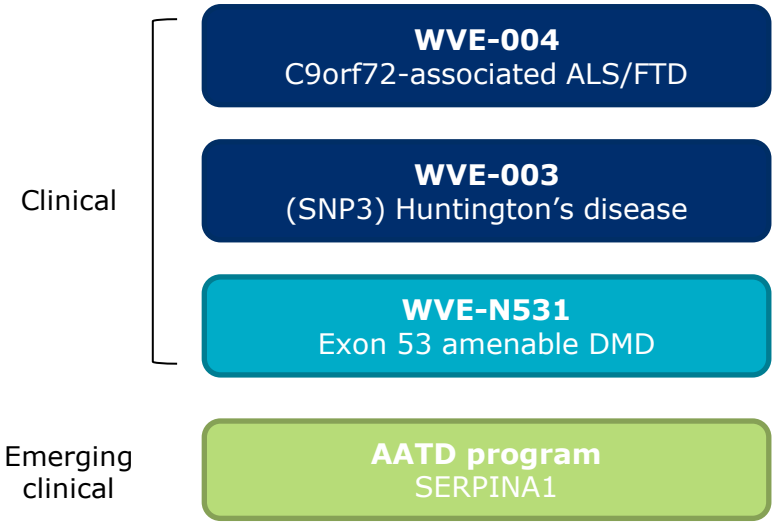
Mike Panzara, MD, MPH

Chief Medical Officer,

Head of Therapeutics

Discovery and Development

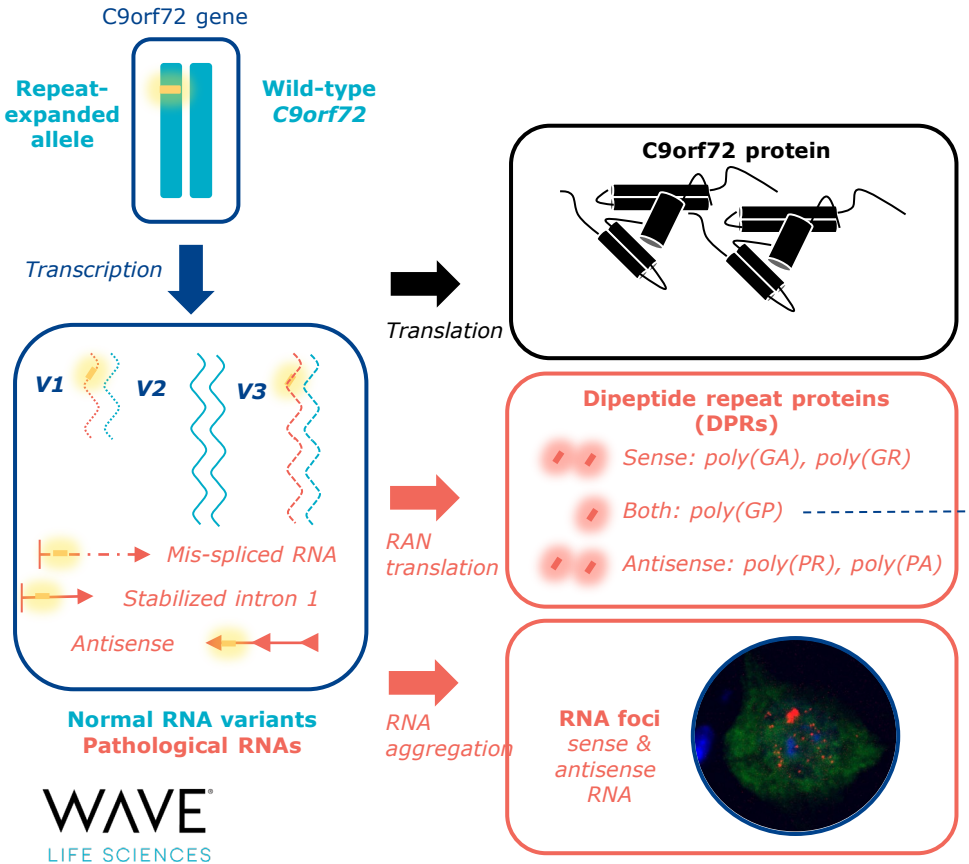
WVE-004: First clinical validation of target engagement in CNS



- ✓ First clinical data demonstrating target engagement in FOCUS-C9 clinical trial single dose cohorts announced April 4, 2022
- Dose escalation ongoing in SELECT-HD clinical trial; Clinical data to enable decision making expected in 2022
- Dose escalation ongoing in initial cohort of open-label clinical trial; Clinical data to enable decision making expected in 2022
- On track to select an AATD AIMer development candidate and initiate IND-enabling toxicology studies in 3Q 2022

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

WVE-004 addresses each aspect of complex, but well described biology of *C9orf72*-associated ALS and FTD



WVE-004 designed to address multiple drivers of toxicity

- ✓ **Variant-selective** oligonucleotide, lowering V1 & V3 in preclinical studies[1]
- ✓ **Preserves** C9orf72 protein expression; does not exacerbate potential loss-of-function driver of disease
- ✓ **Reduces** toxic gain-of-function drivers of disease (RNA foci, DPRs)

Poly(GP) biomarker selected as preferred DPR biomarker

- ✓ Abundant in CNS
- ✓ Most soluble
- ✓ Stable expression
- ✓ Only DPR derived from both sense & antisense RNAs

[1]Liu *et al.*, 2022 *Mol Ther Nuc Acids* doi: 10.1016/j.omtn.2022.04.007

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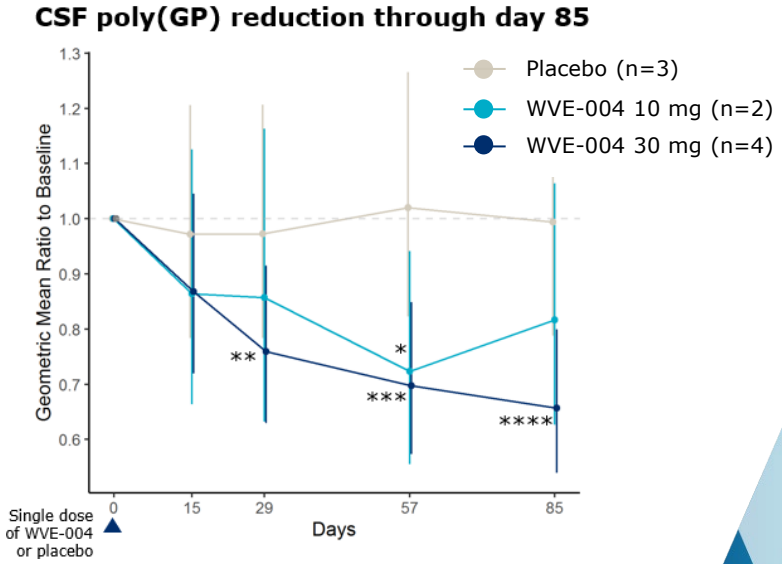
WVE-004 clinical data demonstrate successful translation of preclinical models to clinic

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

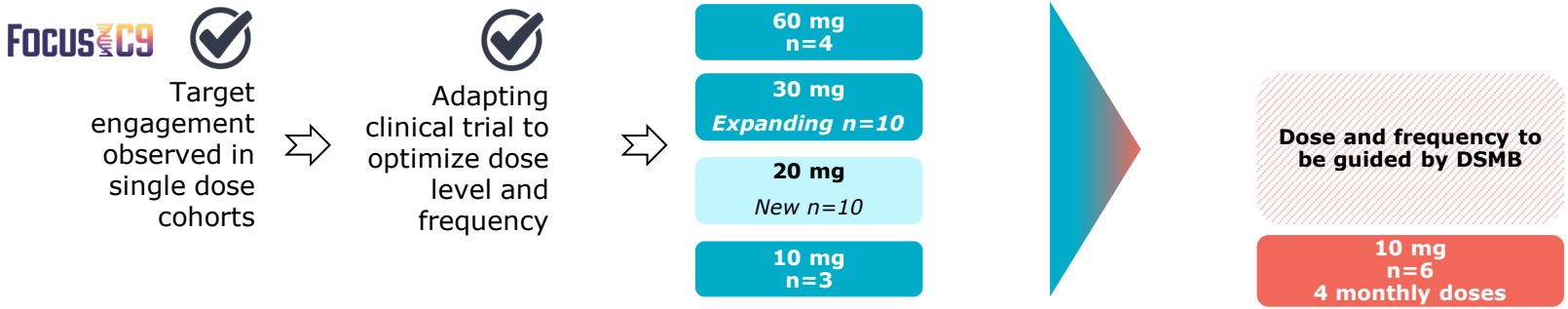
- ✓ Poly(GP) reduction in cortex and spinal cord in transgenic mice with WVE-004
- ✓ Sufficient concentrations of WVE-004 in cortex and spinal cord of NHP for target engagement

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



PK: pharmacokinetic PD: pharmacodynamic; Right: *p=0.020, **p=0.008, ***p=0.001, ****p<0.001, % change from baseline. Mixed model for repeated measures used for all statistical testing

Optimizing dose level and frequency to enable discussions with regulatory authorities later in 2022



- Given poly(GP) reduction with single 30 mg doses that does not appear to have plateaued at day 85, extending observation period and adding additional patients to FOCUS-C9 clinical trial
- Dosing in a multidose cohort (monthly) at 10 mg is well underway
- Planning underway for initiation of an open-label extension (OLE) clinical trial in mid-2022
- Data planned to be presented in oral presentation at ENCALS Meeting (June 1-3, 2022)

Additional single and multidose data for WVE-004 expected throughout 2022

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ENCALS: European Network to Cure ALS

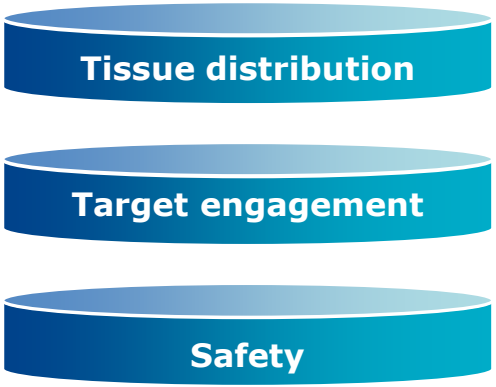
FOCUS-C9 is first example of approach taken with current clinical and preclinical candidates

Key to delivering therapeutic success in CNS

PRISM platform

- ✓ PN backbone modifications in the setting of chiral control and other PRISM advancements improve potency, tissue distribution, and duration of effect
- ✓ Increased emphasis on translational pharmacology

Rational design



Innovative development plans

Selection of relevant biomarkers, clinical endpoints, study duration, dosing regimen

Right target for disease	Right patient population

Current and future unmet need

FOCUS-C9 update provided proof-of-concept clinical data with an effect on a relevant biomarker, even at the starting dose

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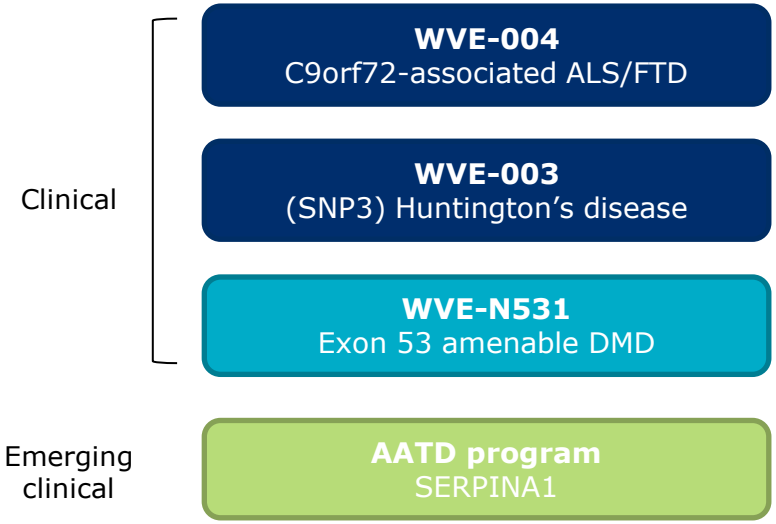
Clinical trials in HD and DMD on track for first data in 2022; AATD program advancing towards clinic



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Kyle Moran

Chief Financial Officer

First quarter 2022 financial results

	Three Months Ended March 31, 2022	Three Months Ended March 31, 2021
Figures are in thousands, except per share amounts		
Revenue	$1,750	$ --
Operating Expenses:		
Research and Development	27,470	33,393
General and Administrative	12,374	10,078
Total Operating Expenses	39,844	43,471
Net Loss from Operations	(38,094)	(43,471)
Total Other Income, Net	280	1,007
Income Tax Provision, net	--	--
Net Loss	($37,814)	($42,464)
Net Loss per Share	**($0.62)**	**($0.86)**

As of March 31, 2022 **Ordinary Shares:** 60.9 million **Cash, Cash Equivalents & Short-Term Investments:** $111.7 million

Wave expects that its existing cash, cash equivalents and short-term investments will enable the company to fund its operating and capital expenditure requirements into 2Q 2023.

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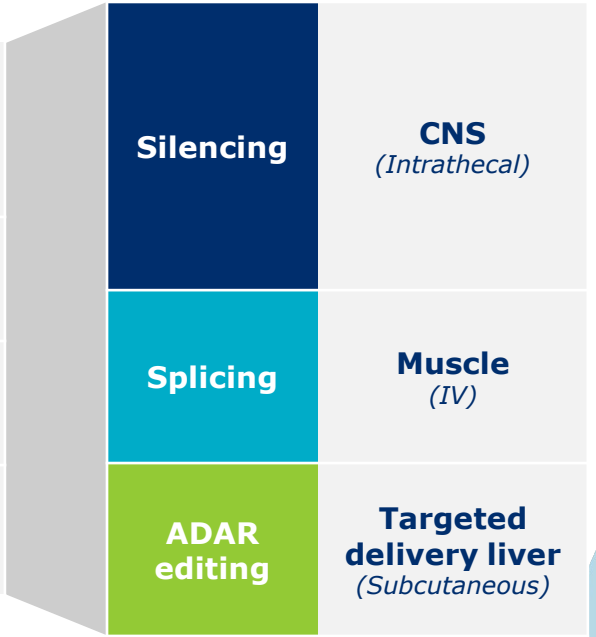
Paul Bolno, MD, MBA

President and CEO

Delivered first clinical data demonstrating target engagement and translation of PN chemistry in CNS

WVE-004 C9orf72 ALS & FTD	✓ Delivered clinical target engagement data with single doses • Additional single and multidose data throughout 2022 • Discussions with regulatory authorities regarding next phase of development later in 2022
WVE-003 HD SNP3	• Clinical data to enable decision making in 2022
WVE-N531 DMD Exon 53	• Clinical data to enable decision making in 2022
AATD program SERPINA1	• Select an AATD AIMer development candidate and initiate IND-enabling toxicology studies in 3Q 2022



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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