Wave Life Sciences

Fourth Quarter and Full Year 2022 Financial Results and Business Update

March 22, 2023

WAVE
LIFE SCIENCES

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.

WAVE LIFE SCIENCES

WAVE LIFE SCIENCES

Paul Bolno, MD, MBA

President and CEO

Today’s agenda

1. **Recent highlights and business update –** Paul Bolno, MD, MBA, President and CEO
2. **Clinical pipeline progress –** Anne-Marie Li-Kwai-Cheung, Chief Development Officer
3. **Financial results –** Kyle Moran, CFA, Chief Financial Officer
4. **Upcoming pipeline and platform catalysts –** Paul Bolno, MD, MBA, President and CEO
5. **Q&A**

WAVE LIFE SCIENCES

Wave is building the leading RNA medicines company

- Most versatile RNA medicines platform (PRISM™) in the industry – ability to match RNA targets to their optimal modality (**editing**, **splicing**, **silencing**) to best address disease biology
- Best-in-class nucleic acid chemistry applicable across modalities
- Novel therapeutic approaches enabling first- or best-in-class candidates
- Platform learnings and clinical validation continue to increase probability of success

→ **Primed to deliver life-changing medicines so that patients and families can realize a brighter future**

WAVE LIFE SCIENCES

2022 was a transformational year for Wave

Achieved clinical validation of PRISM™ platform	• Highest exon skipping (53%) seen in any DMD clinical trial (WVE-N531) • Potent, durable target engagement in CNS after single doses of WVE-003 (HD) or WVE-004 (ALS/FTD) • Translation from preclinical models – accurately predicted doses that would engage target
Leading position in RNA editing	• WVE-006 selected as first RNA editing development candidate for AATD; IND enabling studies underway • *In vivo* proof-of-concept achieved for new applications of RNA editing "AIMers": upregulation and protein-protein modulation
Growing our high-value pipeline	• Announced transformative collaboration with GSK – expected to add multiple first-in-class programs to Wave pipeline • Continuing buildout of wholly owned pipeline; potential for additional exon skipping programs in DMD, as well as RNA editing and RNAi programs
Well capitalized to execute	• Extended cash runway into 2025, including GSK upfront ($170M in cash and equity) • Executing on GSK collaboration – potential to deliver up to $3.3B in milestones (not included in cash runway)

WAVE LIFE SCIENCES

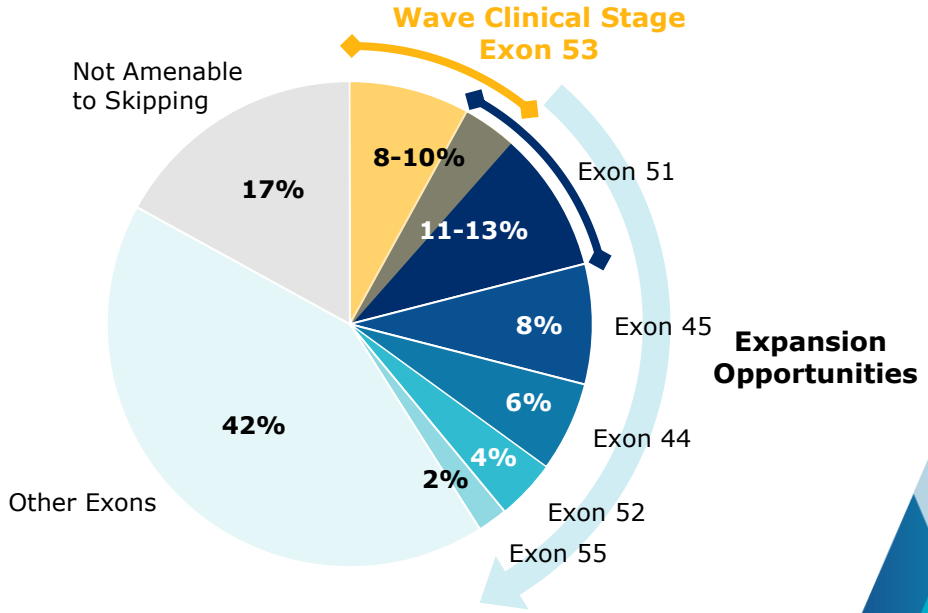
AIMers: Wave's A-to-I(G) RNA base editing oligonucleotides

WVE-N531 gives line-of-sight to significant commercial opportunity

Wave chemistry resulting in differentiated profile for Wave exon skipping oligonucleotides

- Observed 53% exon skipping after three consecutive doses of WVE-N531
  - Potential to result in meaningful levels of functional dystrophin
  - No peptide or antibody conjugates
- Positive WVE-N531 dystrophin data opens up significant commercial opportunity for Wave
- Also enables multi-exon development strategy to build a DMD portfolio
  - *In vitro* exon skipping data generated with PN-modified compounds across multiple exons

Potential for WVE-N531 to enable multi-exon opportunity



WAVE LIFE SCIENCES

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

AIMers provide unparalleled mechanistic dexterity to address diseases in novel ways

WVE-006 for AATD (GalNAc-AIMer)

Poised to be first RNA editing candidate to enter the clinic

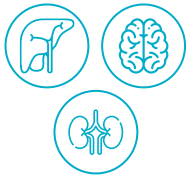
Restoration of M-AAT protein validates:

- ✓ RNA editing in AATD
- ✓ RNA editing as new therapeutic modality

Restore or correct protein function

Expanding in multiple therapeutic applications beyond precise correction of single base mutations, including **upregulation** and **modulation of protein interactions**

Hepatic
CNS
Renal



Monogenic rare diseases

Prevalent diseases

Benefits of AIMers as a modality:

- ✓ Efficient ADAR recruitment
- ✓ Stability, durability
- ✓ Ease of delivery (GalNAc, free uptake)
- ✓ Low risk of off-target or bystander edits
- ✓ Maintains integrity of the genome

New wholly owned programs with preclinical data to be announced starting in 2023

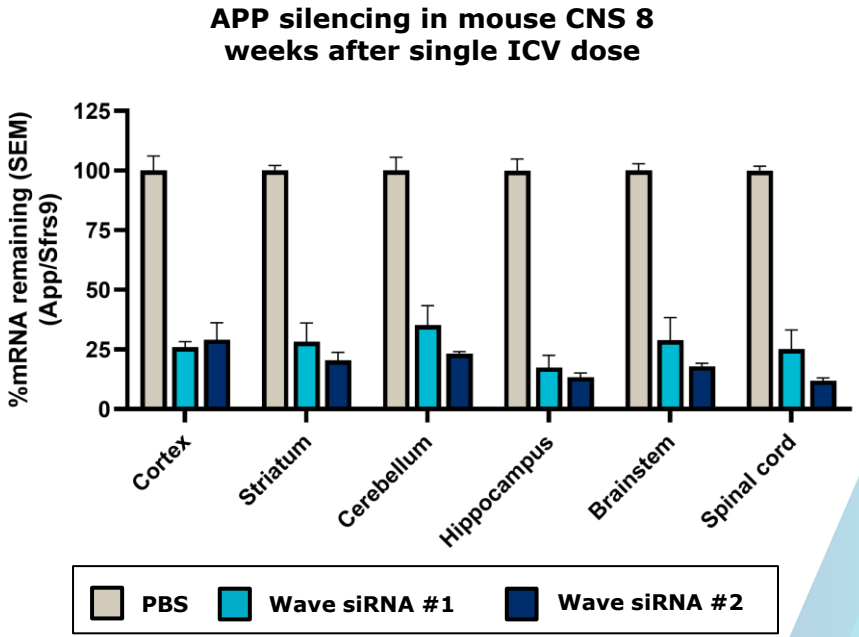
WAVE LIFE SCIENCES

AIMer: A-to-I(G) RNA base editing oligonucleotides; AATD: Alpha-1 antitrypsin deficiency; AAT: Alpha-1 antitrypsin

Potential for best-in-class RNAi enabled by PRISM platform

PRISM chemistry enhances Ago2 loading and tissue exposure – data indicate broad distribution and improvements in potency and durability

- ✓ GalNAc-siRNA led to unprecedented potency and durability in hepatic silencing in mice across two targets: mouse **Ttr** and human **HSD17B13**
- ✓ First *in vivo* study of unconjugated siRNAs demonstrated 70-90% **APP** silencing across six brain regions in mouse CNS at 8 weeks



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 the administration. Taqman qPCR assays were used for RNA PD, relative fold changes of *App* to *Sfrs9* mRNA normalized to percentage of PBS group. All treated group show $P \leq 0.0001$ compared to PBS group in 2way ANOVA.

GSK collaboration expected to yield substantial value for Wave

Maximizes commercial opportunities for WVE-006

- ✓ GSK prioritized as partner given expertise in global clinical development, commercialization and respiratory outcomes studies
- ✓ Wave maintains control of program through first-in-patient study for AATD

Unlocks additional PRISM capabilities & modalities

- ✓ Collaboration may leverage all Wave modalities, including growing RNA editing and RNAi capabilities
- ✓ Opportunities with GalNAc in liver, as well as across disease areas outside liver

Accelerates transformative RNA therapeutics

- ✓ GSK novel insights on genetic targets enables multitude of first-in-class opportunities – both rare and prevalent indications
- ✓ Ongoing milestone payments (up to $3.3B) support buildout of differentiated Wave pipeline

WAVE LIFE SCIENCES

Broad range of addressable targets and markets for Wave

Additional Exons for DMD

- Multi-exon portfolio unlocked with dystrophin data for WVE-N531
- >80% of DMD population estimated to be amenable to exon skipping
- *In vitro* data generated for PN-modified compounds across multiple exons beyond exon 53

Splicing

Inborn Errors of Metabolism

- Rare genetic disorders leading to accumulation of toxic metabolites
- Upregulation approaches may allow mutation-independent strategies that increase total addressable patient populations
- Many addressable through GalNAc-mediated delivery

RNA Editing (Correction, Upregulation)

Cardiometabolic Conditions

- Genetically validated targets, including hepatokines
- Highly prevalent conditions affecting >10% of adults in the US and Europe
- Associated with significant mortality and economic burden
- Addressable through GalNAc-mediated delivery

RNA Editing and RNAi

Potential to expand wholly owned pipeline in variety of tissues, including CNS

WAVE LIFE SCIENCES

Growing portfolio of differentiated RNA medicines

Program	Discovery	Preclinical	Clinical	Rights	Patient Population (US & Europe)
SPLICING					
WVE-N531 Exon 53 (DMD)			Phase 1/2	100% global	2.3K
Other exons (DMD)				100% global	Up to 18K
RNA EDITING					
WVE-006 SERPINA1 (AATD)				GSK exclusive global license	200K
Multiple				100% global	-
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					
Multiple				100% global	-

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

WAVE LIFE SCIENCES

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

WAVE LIFE SCIENCES

Anne-Marie Li-Kwai-Cheung

Chief Development Officer

Executing on our differentiated pipeline

WVE-N531 Exon 53-amenable Duchenne muscular dystrophy	**WVE-006 (GalNAc AIMer)** Alpha-1 antitrypsin deficiency	**WVE-003 (allele-selective)** SNP3 Huntington's disease	**WVE-004** C9orf72-associated ALS/FTD
✓ Announced positive PoC data in Dec. 2022	✓ IND-enabling studies underway	✓ Delivered first clinical data in Sept. 2022	✓ Delivered first clinical data in Apr. 2022
• Initiating Part B (Phase 2) to evaluate dystrophin	• CTA filings expected 2H 2023	• SAD cohort expansion ongoing	✓ Enrollment in SAD and MAD cohorts completed
		• Data expected 1H 2023	• Data expected 1H 2023

Therapeutic modality: Splicing; RNA editing (AIMers); Silencing (antisense)

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; ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia

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

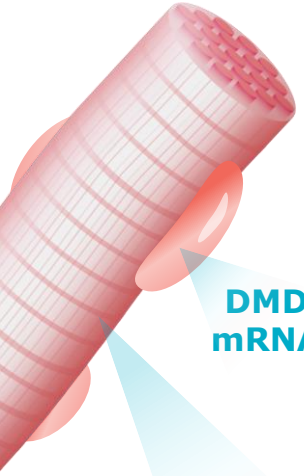
42 µg/g = 6.1 µM

BLQ: Below level of quantification (1%)

WAVE LIFE SCIENCES

Dystrophin protein is expected to accumulate following prolonged exposure

Muscle Fiber

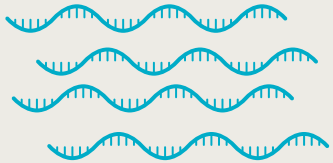


DMD mRNA

Dystrophin protein

Healthy Tissue

DMD transcripts are **long**, **rare**, **nominally stable**, and require **prolonged transcription**, making them fragile by nature



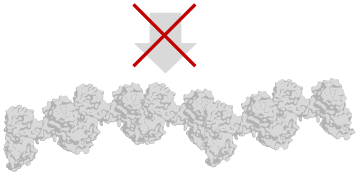
~10 copy number;
20-40 transcripts

DMD

Untreated

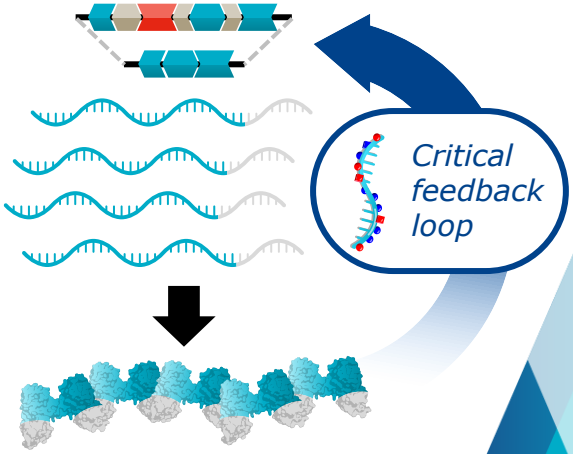
Nonsense-mediated decay **destabilizes** transcripts and further **limits their numbers**

0 copy number;
10 transcripts



Treated

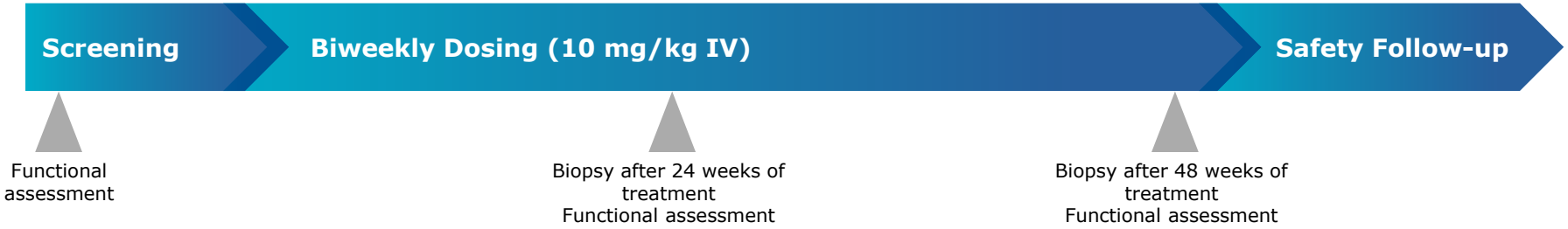
Exon skipping via **persistent WVE-N531** exposure **increases** initiation, copy number, and stability



WAVE LIFE SCIENCES

Hildyard *et al.*, 2020 *PLoS One* doi: 10.1371/journal.pone.0239467; Tennyson *et al.*, 1995 *Nat Genetics* doi: 10.1038/ng0295-184; Tennyson *et al.*, 1996. *Nuc Acids Res* doi: 10.1093/nar/24.15.3059

Initiating Part B of WVE-N531 clinical trial



- 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 expected in 2024

WAVE LIFE SCIENCES

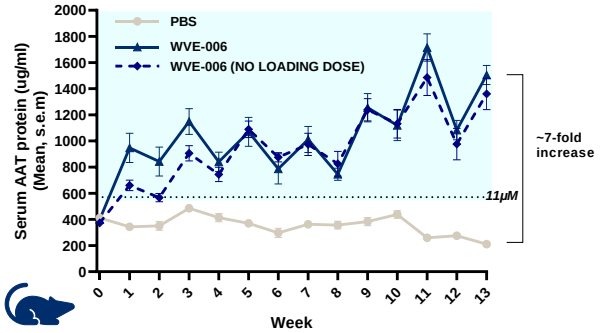
IV: intravenous; NSAA: North star ambulatory assessment

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

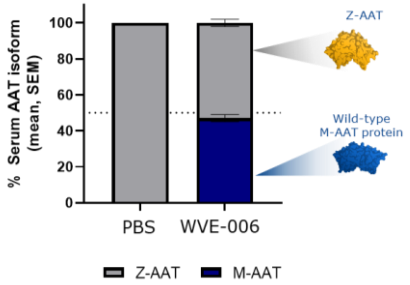
Increased AAT protein in NSG-PiZ mice

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



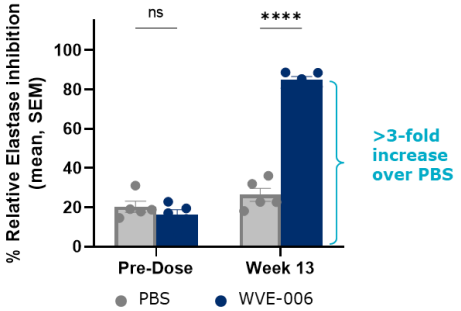
Confirmed restored wild-type M-AAT protein

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



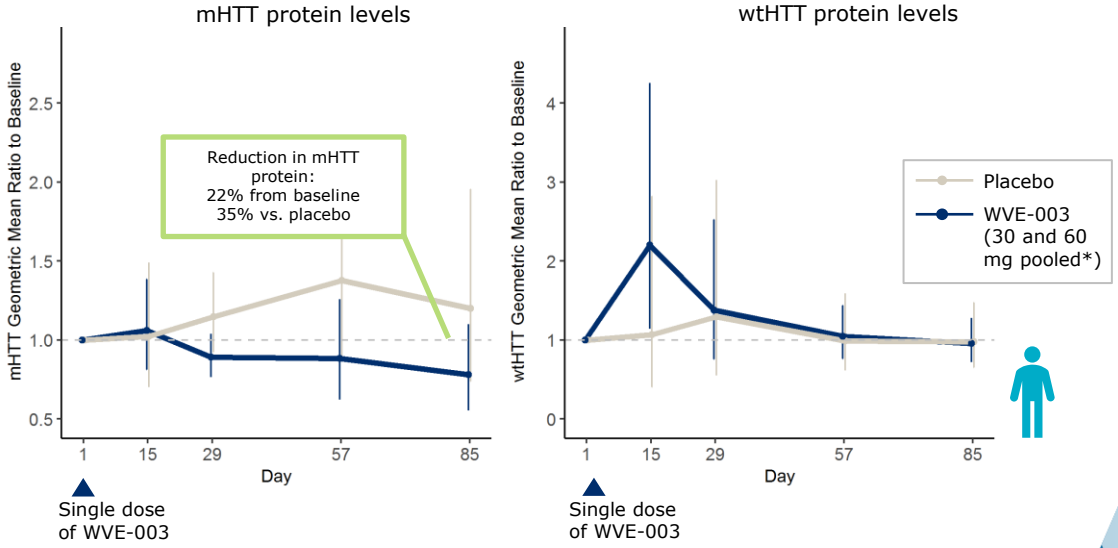
CTA submissions for first-in-human study expected in 2H 2023

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

WVE-003 in HD: Delivered target engagement data in Q3 2022

- mHTT protein reductions observed in single dose cohorts (Sep. 2022)
- wtHTT protein levels appear consistent with allele-selectivity
- Generally safe and well-tolerated
- **Data expected in 1H 2023 from following cohorts:**
  - 30 mg single dose
  - 60 mg single dose
  - 90 mg single dose

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

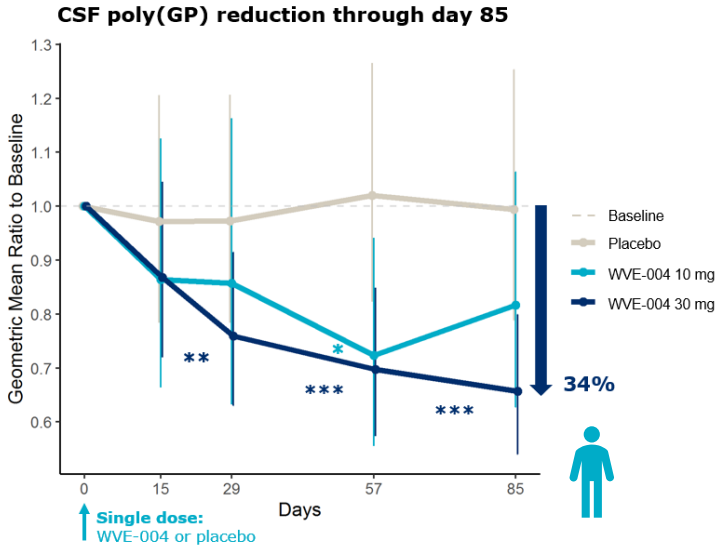


mHTT: mutant huntingtin protein; wtHTT: wild-type huntingtin protein
*Pooled considering no apparent dose response between 2 cohorts; Data cut-off: August 29, 2022

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
- **Study ongoing with 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

WAVE LIFE SCIENCES

Kyle Moran, CFA

Chief Financial Officer

Fourth quarter 2022 financial results

Figures are in thousands, except per share amounts	Three Months Ended December 31, 2022	Three Months Ended December 31, 2021
Revenue	$1,239	$1,765
Operating Expenses:		
Research and Development	31,078	25,761
General and Administrative	13,724	12,114
Total Operating Expenses	44,802	37,875
Net Loss from Operations	(43,563)	(36,110)
Total Other Income, Net	535	1,121
Income Tax Benefit (Provision)	(681)	204
Net Loss	($43,709)	($34,785)
Net Loss per Share	**($0.47)**	**($0.61)**

As of Dec 31, 2022	**Ordinary Shares Outstanding:** 86.92 million	**Cash and Cash Equivalents:** $88.5 million
In Q1 2023	**Ordinary Shares Issued to GSK:** 10.68 million	**Cash from GSK Collaboration:** $170.0 million

WAVE LIFE SCIENCES

Wave expects that its cash and cash equivalents will be sufficient to fund operations into 2025.

WAVE LIFE SCIENCES

Paul Bolno, MD, MBA

President and CEO

Delivering on pipeline and platform catalysts

ANTISENSE SILENCING

WVE-003 for HD
Only clinical stage wtHTT-sparing approach

WVE-004 for ALS/FTD
Variant-selective approach for C9orf72

Data expected 1H 2023

Enables discussion on next steps with Takeda

SPLICING

WVE-N531 for DMD
Potential best-in-class approach with highest exon skipping reported

Part B dosing expected in 2023; data expected in 2024

Expansion opportunities in other exons, as well as other muscle diseases and CNS

RNA EDITING

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

RNAi

Newest modality in Wave platform
Preclinical data suggest best-in-class potential for Wave RNAi capability

Hepatic, CNS and beyond

DISCOVERY PIPELINE & COLLABORATIONS

New wholly owned programs with preclinical data expected to be announced starting in 2023

Research support funding and potential for milestone payments from GSK collaboration (2023 and beyond)

WAVE LIFE SCIENCES

Q&A

WAVE®
LIFE SCIENCES

For more information:

Kate Rausch, Investor Relations
InvestorRelations@wavelifesci.com
617.949.4827

WAVE
LIFE SCIENCES