



Wave Life Sciences

Third Quarter 2022 Earnings

November 10, 2022

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Forward-looking statements

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Paul Bolno, MD, MBA
President and CEO

Today's agenda

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Recent business highlights - Paul Bolno, MD, MBA, President and CEO

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Clinical pipeline update – Anne-Marie Li-Kwai-Cheung, Chief Development Officer

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3Q 2022 financial results – Kyle Moran, CFA, CFO

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Closing remarks and upcoming milestones – Paul Bolno, MD, MBA, President and CEO

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Q&A

Third quarter 2022 and recent highlights

Continued clinical translation of PN chemistry

- Positive update announced in HD with single doses of WVE-003
- Clinical data from DMD trial expected in 4Q 2022



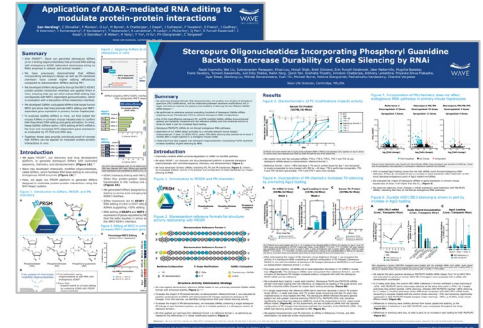
First-in-class AATD RNA editing candidate advancing

- RNA editing for AATD highlighted in virtual event
- Preclinical data supporting WVE-006 presented at OTS



Innovative oligonucleotide platform presentations

- Preclinical *in vivo* gene upregulation data with AIMers (ESGCT)
- siRNA designs with PRISM chemistry (OTS)





Anne-Marie Li-Kwai-Cheung
Chief Development Officer

Executing on clinical and emerging clinical programs to reach key milestones

Clinical

IND-enabling

WVE-003
(allele-selective)
SNP3
Huntington's disease

- ✓ Delivered first clinical data in 3Q 2022

WVE-N531
Exon 53-amenable
Duchenne muscular
dystrophy

- ✓ Initiated multidose in 3Q 2022

WVE-004
C9orf72-associated
ALS/FTD

- ✓ Delivered first clinical data in 2Q 2022
- ✓ Initiated open-label extension trial in 4Q 2022

WVE-006
(GalNAc AIMer)
Alpha-1 antitrypsin
deficiency

- ✓ Selected development candidate in 3Q 2022
- ✓ IND-enabling studies underway



WVE-003: Only investigational HD therapy in clinical development designed to lower mHTT while sparing wtHTT

wtHTT supports healthy brain function, especially in the context of stress



Regulates synaptic plasticity



Supports synaptic protein transport



Promotes neuronal survival



Supports cilia and CSF circulation

WVE-003

Unique and innovative wildtype HTT-sparing oligonucleotide

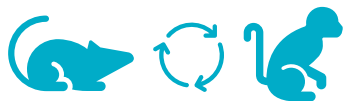
Delivered to CNS without invasive surgical procedures

No complex delivery vehicles required (e.g. AAV)

Designed with next-generation PN chemistry

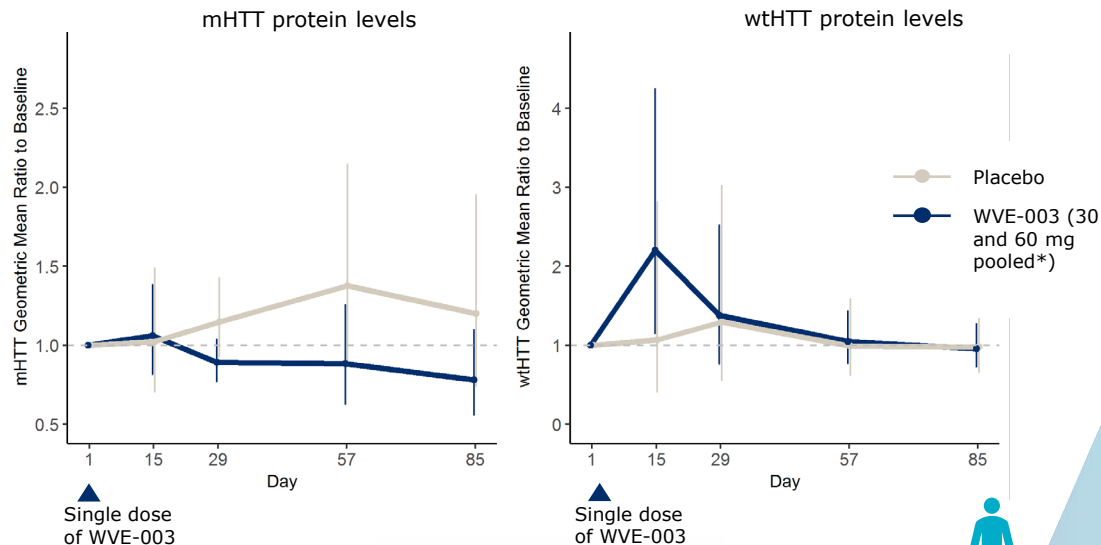
Initial clinical results indicating allele-selective target engagement suggests translation of preclinical data

PK/PD modeling using preclinical *in vivo* models



- ✓ Allele selectivity (Hu97/18 mice)
- ✓ mHTT reduction in cortex and striatum (transgenic mice)
- ✓ Concentrations in NHP brain tissues sufficient for target engagement

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



Expanding single dose cohorts to optimize dose level based on initial clinical results



- mHTT protein reductions observed in single dose cohorts
- wtHTT protein levels appear consistent with allele-selectivity
- Generally safe and well-tolerated



- Adapting clinical trial to optimize dose level



SELECT  **HD**

90 mg
Expanding cohort

60 mg
Expanding cohort

30 mg
Expanding cohort

Adding patients to each cohort

Additional single-dose biomarker and safety data are expected in 1H 2023

WVE-N531 improved muscle concentrations, exon skipping, function, and overall survival in dKO mouse



dKO mice

- ✓ PN chemistry improved muscle exposure, muscle/respiratory function, and survival over PS/PO compounds
- ✓ Muscle concentration improvements correlated with exon skipping activity

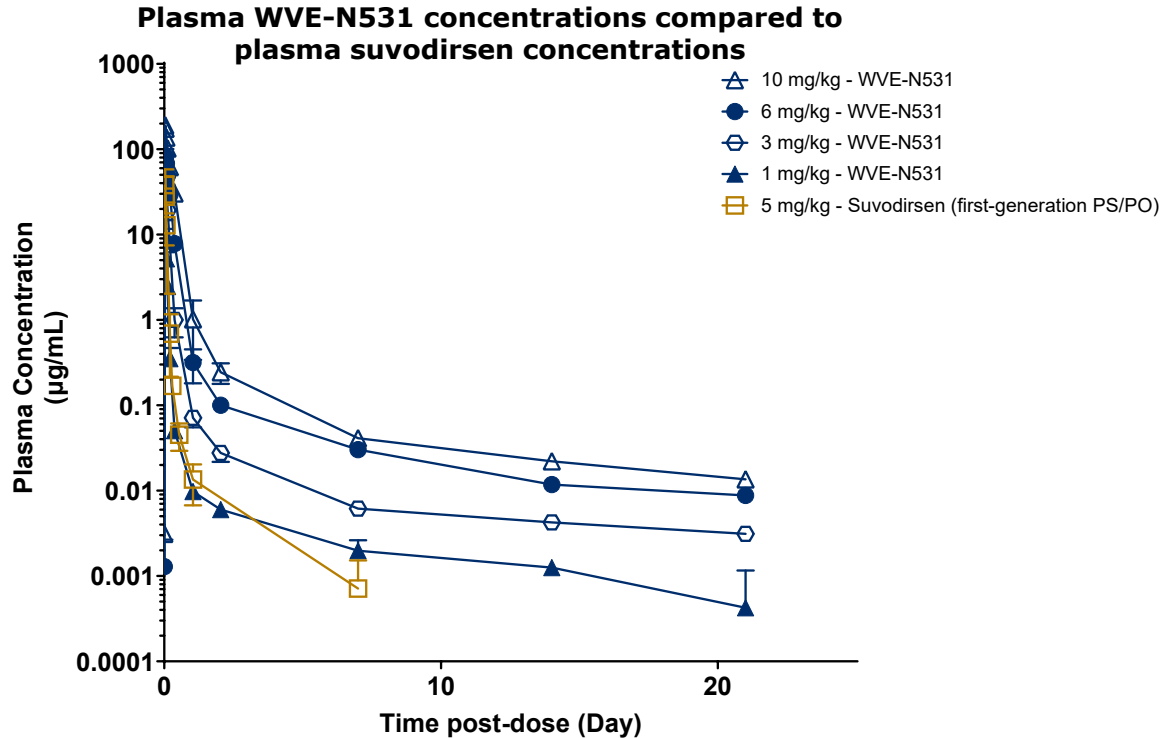


NHPs

- ✓ Plasma and muscle concentrations of WVE-N531 significantly higher than suvodirsen (1st-gen PS/PO)
- ✓ WVE-N531 led to exon skipping at significantly lower doses than suvodirsen

Top doses evaluated represent human-equivalent level in the range explored in preclinical dKO mouse

Higher plasma concentrations

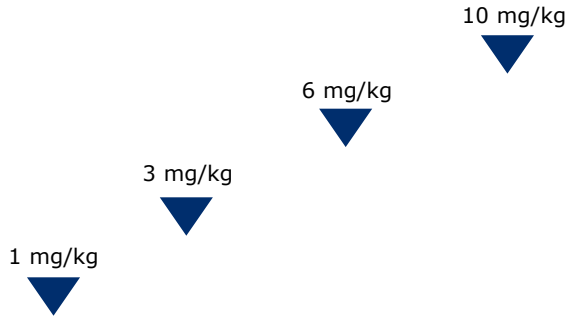


Dosing underway with multiple doses of WVE-N531

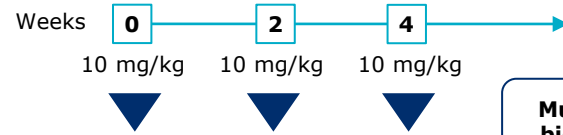
Ascending intra-patient single doses

3 additional doses every other week

Initial cohort
• Boys with DMD amenable to exon 53 skipping



▼ Dose WVE-N531



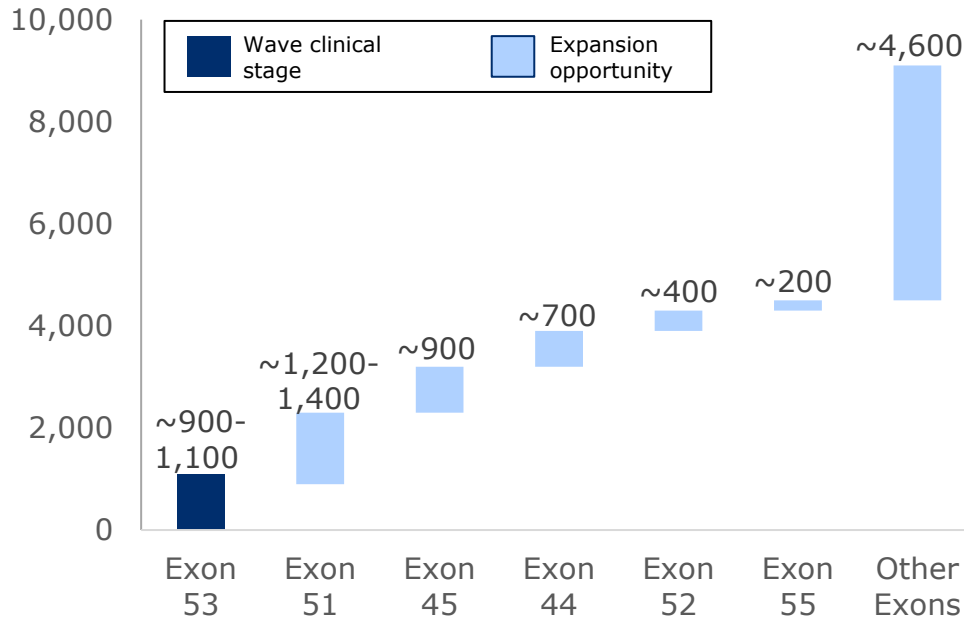
Data to include:

- WVE-N531 muscle concentrations
- WVE-N531 localization
- Exon skipping
- Dystrophin protein

Clinical data, including muscle biopsies, expected in 4Q 2022

Potential to expand addressable patient population with additional exon skipping programs

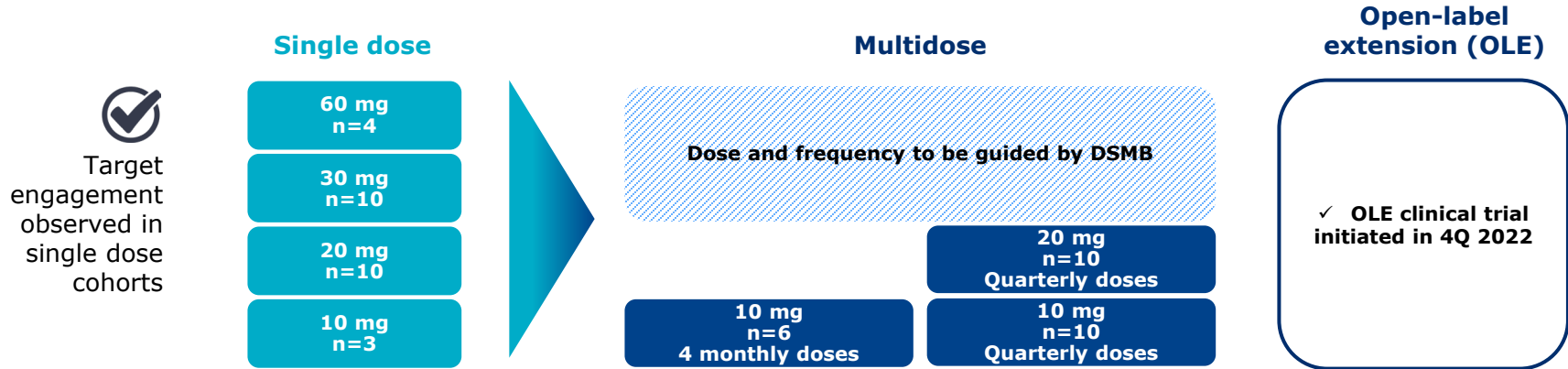
DMD population in US with genetic mutations amenable to exon skipping



- *In vitro* exon skipping data generated with PN-modified compounds across multiple exons
- Potential for multi-exon development strategy to build a DMD portfolio

Dosing ongoing in FOCUS-C9 clinical trial with multiple doses of WVE-004

FOCUS-C9



Data from all cohorts in the FOCUS-C9 trial are expected in 1H 2023

WVE-006: IND-enabling studies ongoing to support CTA submissions in 2023

WVE-006 preclinical data highlighted at Sept. 28 "Towards the Clinic: Spotlight on RNA Editing for AATD" virtual event and OTS Annual Meeting



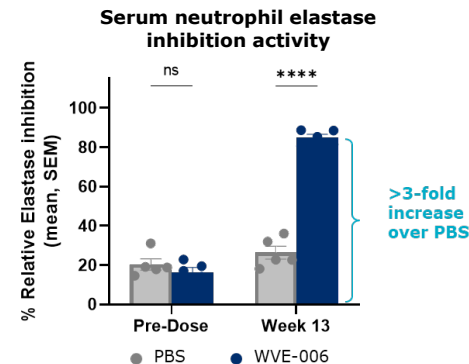
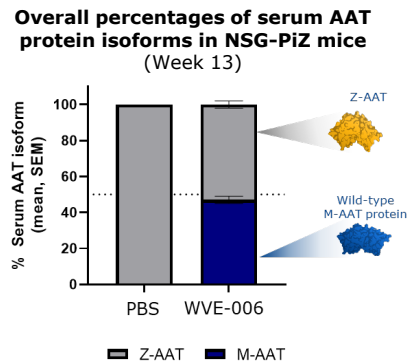
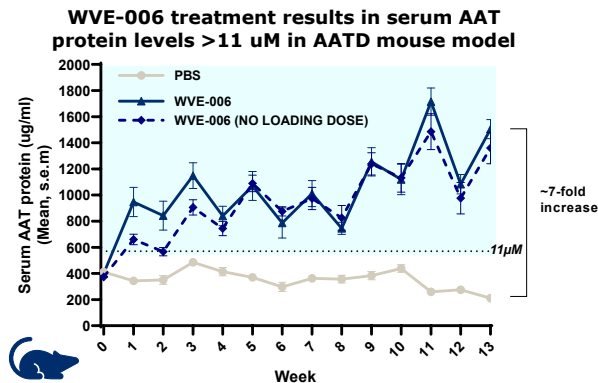
Increased AAT protein in NSG-PiZ mice



Confirmed restored wild-type M-AAT protein



Demonstrated functionality of M-AAT protein



WVE-006 is a potential first- and best-in-class candidate for AATD



Kyle Moran, CFA
Chief Financial Officer

Third quarter 2022 financial results

	Three Months Ended September 30, 2022	Three Months Ended September 30, 2021
<i>Figures are in thousands, except per share amounts</i>		
Revenue	\$285	\$36,423
Operating Expenses:		
Research and Development	27,575	31,086
General and Administrative	11,609	12,944
Total Operating Expenses	39,184	44,030
Net Loss from Operations	(38,899)	(7,607)
Total Other Income (Expense), Net	(105)	1,377
Income Tax Provision	--	--
Net Loss	(\$39,004)	(\$6,230)
Net Loss per Share	(\$0.42)	(\$0.12)
As of Sept 30, 2022	Ordinary Shares: 86.8 million Cash, Cash Equivalents and Short-term Investments: \$122.0 million	



Paul Bolno, MD, MBA
President and CEO

Unlocking new biology using AIMers to activate pathways and upregulate expression



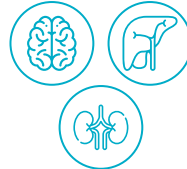
Restore or correct protein function

WVE-006
(GalNAc AIMer)
AATD

AIMer pipeline expansion

Discovery work ongoing in CNS, hepatic and renal

CNS
Hepatic
Renal



More prevalent disease indications

Monogenic rare diseases



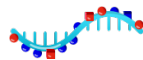
AIMers provide dexterity, with applications beyond precise correction of genetic mutations, including upregulation

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

Steady flow of data updates expected to further inform future opportunities and unlock value

WVE-004 C9orf72 ALS & FTD	<ul style="list-style-type: none">✓ Delivered clinical target engagement data with single doses✓ Initiated OLE clinical trial in 4Q 2022• Data from all cohorts in FOCUS-C9 trial expected in 1H 2023	Silencing	CNS <i>(Intrathecal)</i>	
WVE-003 HD SNP3	<ul style="list-style-type: none">✓ Delivered single-dose clinical data indicating reduction in mHTT with wtHTT preserved, appearing consistent with allele-selectivity• Additional single-dose biomarker and safety data in 1H 2023		Splicing	Muscle <i>(IV)</i>
WVE-N531 DMD Exon 53	<ul style="list-style-type: none">• Clinical data, including muscle biopsies, to enable decision making in 4Q 2022			Targeted delivery liver <i>(Subcutaneous)</i>
WVE-006 AATD	<ul style="list-style-type: none">✓ Selected an AATD AIMER development candidate and initiated IND-enabling activities• Submit clinical trial applications in 2023		ADAR editing	

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Q&A

Realizing a brighter future for people affected by genetic diseases

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