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Wave Life Sciences

Corporate Presentation

March 1, 2019

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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Wave Life Sciences is a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases.

Wave aspires to develop best-in-class medicines across multiple therapeutic modalities using PRISM™, the company's proprietary discovery and drug development platform that enables the precise design, optimization and production of stereopure oligonucleotides.

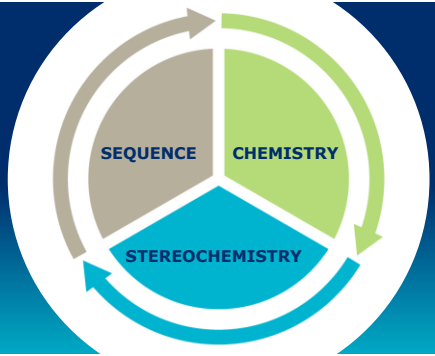
Driven by a resolute sense of urgency, the Wave team is targeting a broad range of genetically defined diseases so that patients and families may realize a brighter future.

PRISM™

Enables Wave to target genetically defined diseases with stereopure oligonucleotides across multiple therapeutic modalities

DESIGN

Unique ability to construct stereopure oligonucleotides with one defined and consistent profile



OPTIMIZATION

A deep understanding of how the interplay among oligonucleotide sequence, chemistry, and backbone stereochemistry impacts key pharmacological properties

Through iterative analysis of *in vitro* and *in vivo* outcomes and artificial intelligence-driven predictive modeling, Wave continues to define design principles that are deployed across programs to rapidly develop and manufacture clinical candidates that meet pre-defined product profiles

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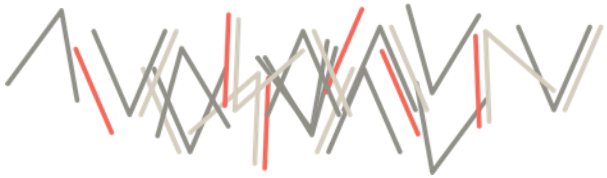
Designing the optimal, stereopure medicine



STANDARD OLIGONUCLEOTIDE APPROACHES

Pharmacologic properties include >500,000 permutations in every dose

↓

Impact:
Unreliable therapeutic effects
Unintended off-target effects

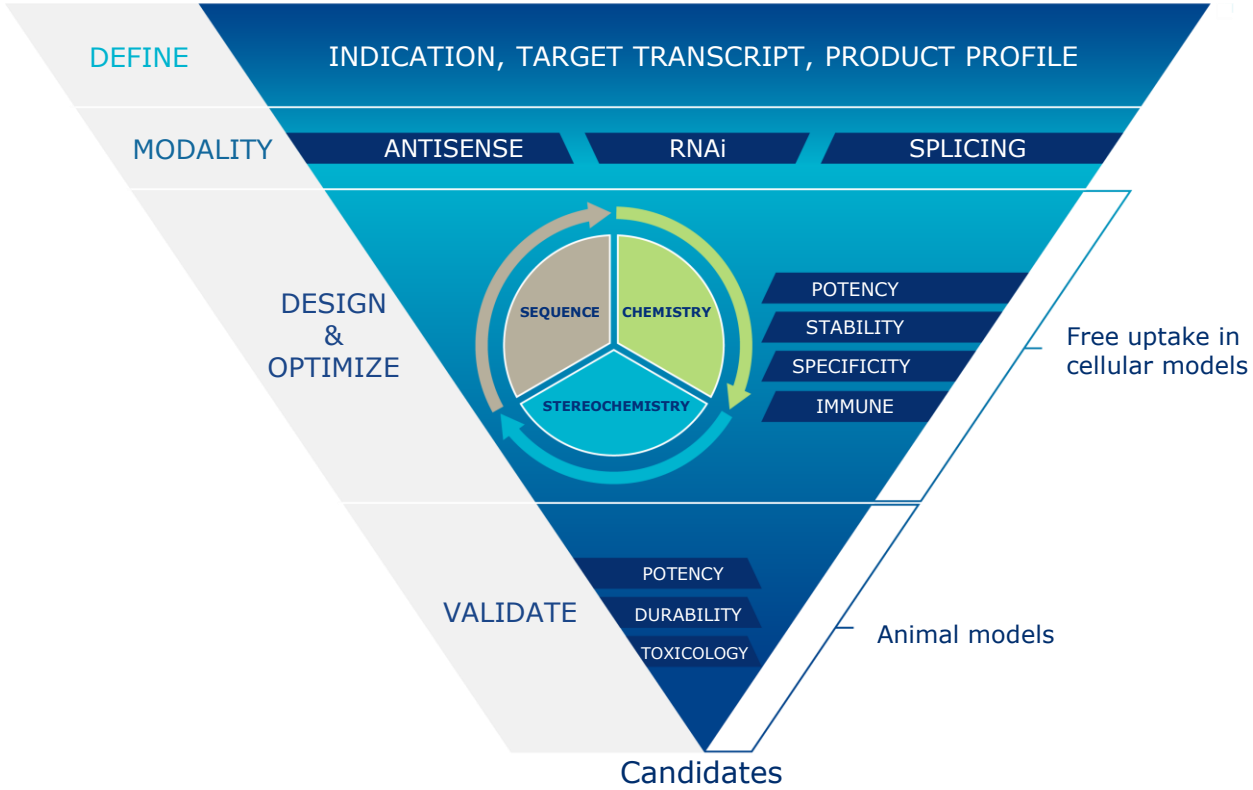
WAVE RATIONAL DESIGN

Control of stereochemistry enables the design and manufacture of oligonucleotides with one defined and consistent profile

↓

Impact:
Potential for best-in-class medicines that can address difficult-to-treat diseases

Creating a new class of oligonucleotides



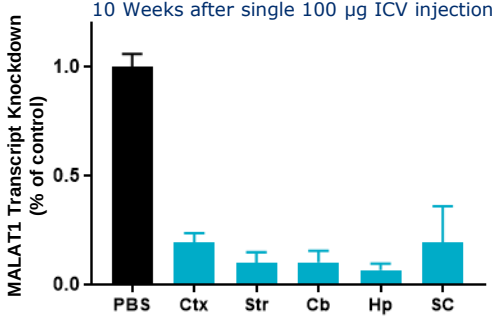
Source: Iwamoto N, et al. Control of phosphorothioate stereochemistry substantially increases the efficacy of antisense oligonucleotides. *Nat Biotechnol*. 2017;35:845-851.

Optimizing potency and durability across multiple tissues

CNS

MALAT1 Transcript Knockdown in Mice

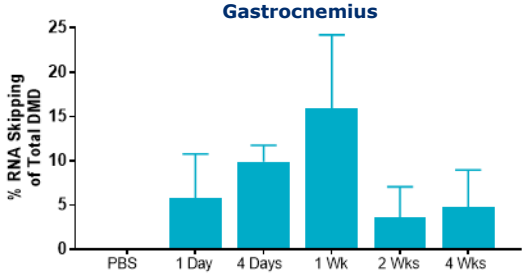
10 Weeks after single 100 µg ICV injection



Muscle

DMD: Percent Skipped Transcript in *mdx*23 Mice

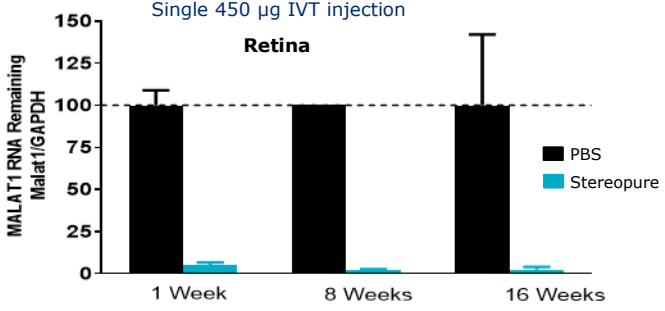
Single 150 mg/kg IV injection



Eye

MALAT1 Knockdown in Non-Human Primates

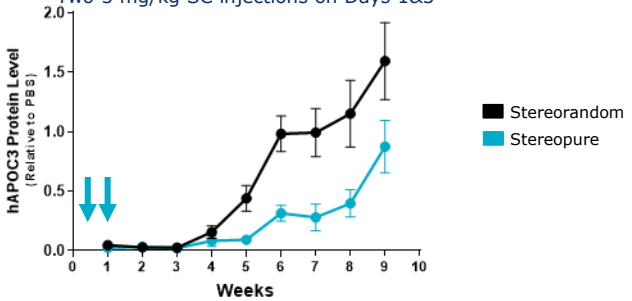
Single 450 µg IVT injection



Liver

Knockdown of Serum hAPOC3 Protein Levels in Mice

Two 5 mg/kg SC injections on Days 1&3

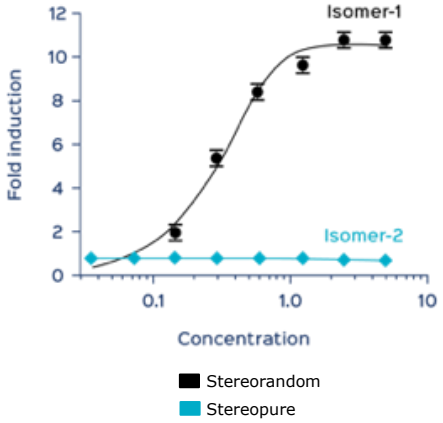


Data represented in this slide from *in vivo* studies. CNS: PBS = phosphate buffered saline; Ctx = cortex; Str = striatum; Cb = cerebellum; Hp = hippocampus; SC = spinal cord. ICV = intracerebral; IVT = intravitreal; IV = intravenous; SC= subcutaneous.

Stereochemistry affects immune activation

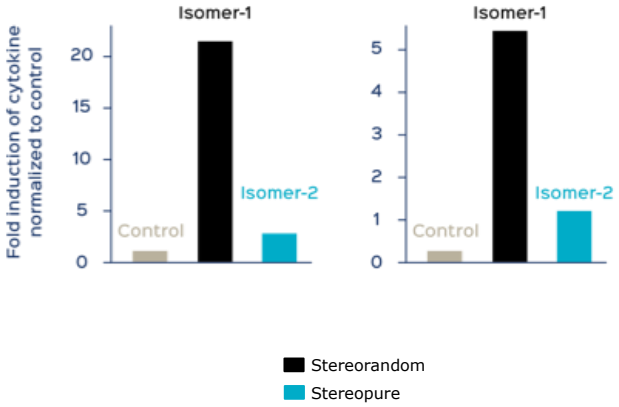
Human TLR9 Activation

Human TLR9 activation assay with 5mC modified CpG containing MOE gapmer



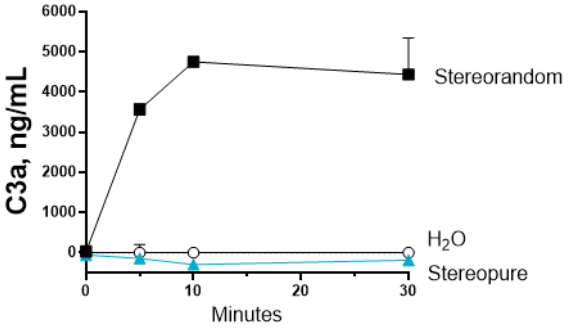
Cytokine Induction

Cytokine induction in human PBMC assay



Complement Activation

Complement activation in non-human primate serum assay



Data represented in this slide from *in vitro* studies. MOE = 2′-O-methoxyethylribose; PBMC = peripheral blood mononuclear cell; TLR9 = toll-like receptor 9.

Pipeline spanning multiple modalities, novel targets

	TARGET	ESTIMATED U.S. PREVALENCE*	MECHANISM	DISCOVERY	CANDIDATE	CLINICAL	WAVE'S COMMERCIAL RIGHTS	PARTNER
MUSCLE								
Duchenne muscular dystrophy	Exon 51	~2,000	E	●	●	Phase 1/OLE	100% Global	—
Duchenne muscular dystrophy	Exon 53	~1,250	E	●	●		100% Global	—
Duchenne muscular dystrophy	Exons 44, 45, 52, 54, 55	~1,500	E	●	○		100% Global	—
Neuromuscular diseases	Multiple		○	●	○		100% Global	—
CNS								
Huntington's disease	mHTT SNP1	~10k / ~35k	A	●	●	Phase 1b/2a	50% Global	Takeda
Huntington's disease	mHTT SNP2	~10k / ~35k	A	●	●	Phase 1b/2a	50% Global	Takeda
Huntington's disease	mHTT SNP3	~ 8k / ~ 30k	A	●	○		50% Global	Takeda
Amyotrophic lateral sclerosis	C9orf72	~1,800	A	●	●		50% Global	Takeda
Frontotemporal dementia	C9orf72	~7,000	A	●	●		50% Global	Takeda
Spinocerebellar ataxia 3	ATXN3	~4,500	S	●	●		50% Global	Takeda
CNS diseases	Multiple†		○	●	○		Milestones & Royalties	Takeda
OPHTHALMOLOGY								
Retinal diseases	RHO, USH2A, ABCA4, CEP290	~10,000	○	●	○		100% Global	—
HEPATIC								
Metabolic liver diseases	APOC3 and Multiple (4)‡		S	●	○		Milestones & Royalties	Pfizer

(S) = silencing. (A) = allele-specific silencing. (E) = exon skipping. OLE = Open-label extension.

*Estimates of U.S. prevalence and addressable population by target based on publicly available data and are approximate; for Huntington's disease, numbers approximate manifest and pre-manifest populations, respectively.
† During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
‡ Pfizer has nominated four undisclosed targets in addition to APOC3.

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Duchenne Muscular Dystrophy (DMD)

DMD: a progressive, fatal childhood disorder

- Fatal, X-linked genetic neuromuscular disorder characterized by progressive, irreversible loss of muscle function, including heart and lung
- Genetic mutation in dystrophin gene prevents the production of dystrophin protein, a critical component of healthy muscle function
- Symptom onset in early childhood; one of the most serious genetic diseases in children worldwide
- Current disease modifying treatments have demonstrated minimal dystrophin expression and clinical benefit has not been established
- Impacts 1 in every 5,000 newborn boys each year; 20,000 new cases annually worldwide

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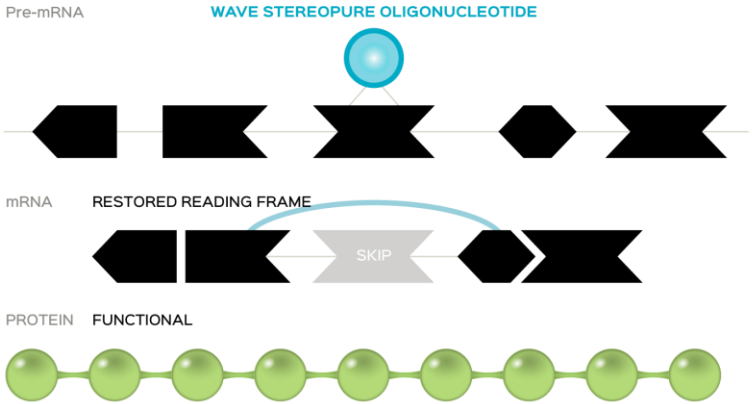
Source: Parent Project Muscular Dystrophy. About Duchenne & Becker muscular dystrophy. Available at: https://www.parentprojectmd.org/care/for-healthcare-providers/. Accessed: November 2, 2018.

Wave approach: stereopure exon skipping oligonucleotide

Exon skipping



Potential benefits of an oligonucleotide approach to treating a lifelong disease

- Chronic administration may better address high muscle cell turnover and need for broad and durable distribution
- Entry into cells, including progenitor cells, via free-uptake
- Production of functional dystrophin protein, not micro-dystrophin
- Scalable manufacturing

Exon skipping with stereopure oligonucleotides has the potential to enable production of meaningful levels of functional dystrophin which is expected to result in therapeutic benefit

Sources: Arnett ALH, et al. *Mol Ther Methods Clin Dev.* 2014;1:14038. doi:10.1038/mtm.2014.38. Counsell JR, et al. *Sci Rep.* 2017;7:79. doi: 10.1038/s41598-017-00152-5. Duan D. *Mol Ther.* 2018;25:2337-2356. Martinsen B, Dreyer P. *Open Nurs Jrnl.* 2016;10:131-138. Stitelman DH, et al. *Mol Ther Methods Clin Dev.* 2014;1:14040. doi:10.1038/mtm.2014.40.

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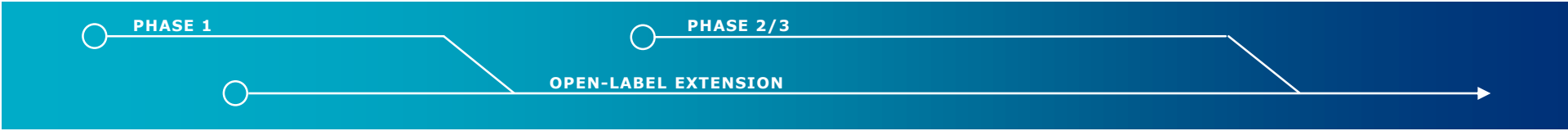
Exon 51: suvodirsen (WVE-210201) clinical program



Phase 1

OBJECTIVE

Determine safety and tolerability profile and select dose(s) for OLE and Phase 2/3

STUDY DESCRIPTION

Phase 1 single ascending dose clinical trial

KEY MILESTONES

- Safety and tolerability profile supports Phase 2/3 initiation
- One dose selected for Phase 2/3 trial, pending final analysis
- Results to be presented at upcoming scientific meetings

Open-Label Extension (OLE)

OBJECTIVE

Provide data that will be an important component of submission for accelerated approval in US

STUDY DESCRIPTION

Multi-dose, open-label study open to patients from Phase 1

KEY MILESTONES

- Initiated in August 2018
- On track to deliver interim analysis of dystrophin expression in H2 2019

Phase 2/3

OBJECTIVE

Provide efficacy and safety data as basis of regulatory submissions globally

STUDY DESCRIPTION

Phase 2/3 clinical trial to assess clinical efficacy and dystrophin expression

KEY MILESTONES

- Selected for FDA pilot program for complex innovative trial designs
- Expect to initiate in 2019

Dystrophin readout expected H2 2019

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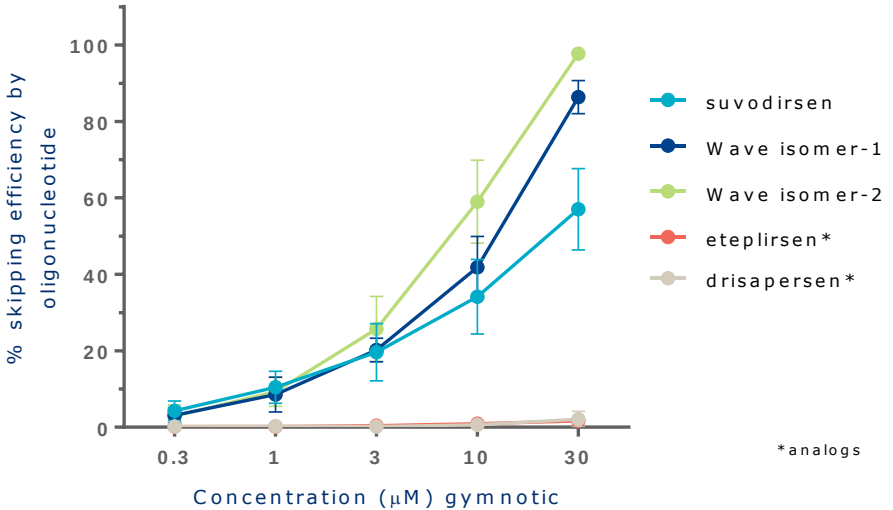
Exon 51: improved skipping efficiency

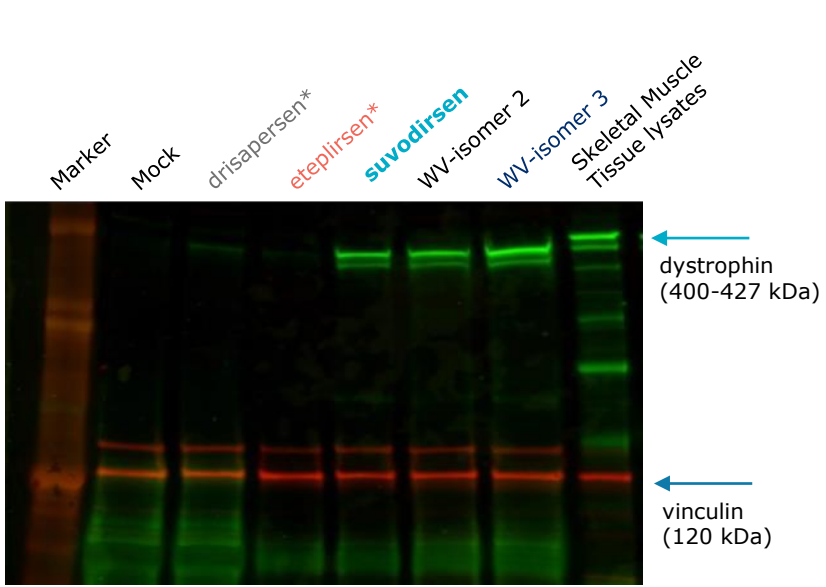
- RNA skipping determined by quantitative RT-PCR
- Wave isomers demonstrated a dose-dependent increase in skipping efficiency *in vitro*
- Free uptake at 10uM concentration of each compound with no transfection agent
- Same foundational stereopure chemistry for Wave isomers; individually optimized to select candidate

Dose Response on Skipping Efficiency
(mRNA, *in vitro*) (4 days)

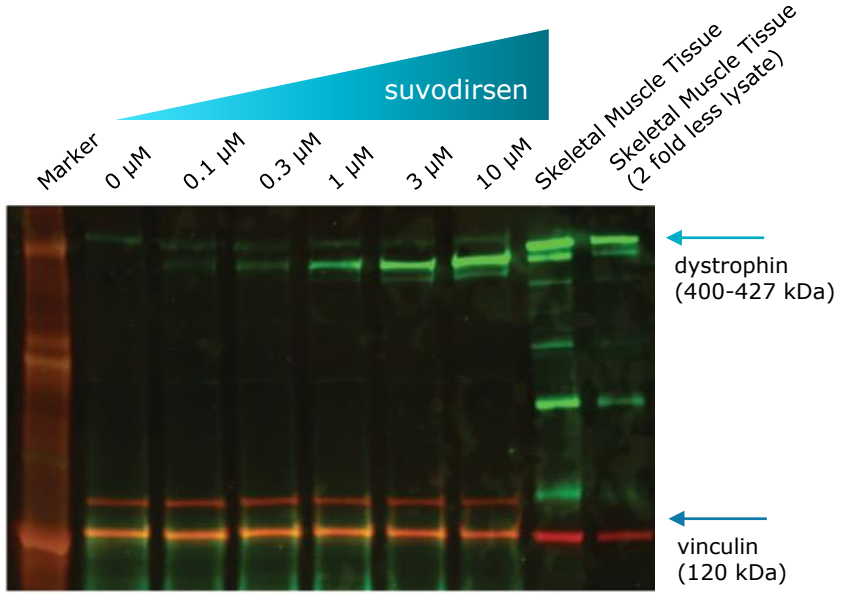


Experimental conditions: Free uptake of ASO in human DMD myoblast cells. Skipping quantified by TaqMan assay.

Exon 51: increased dystrophin restoration



*Analogs

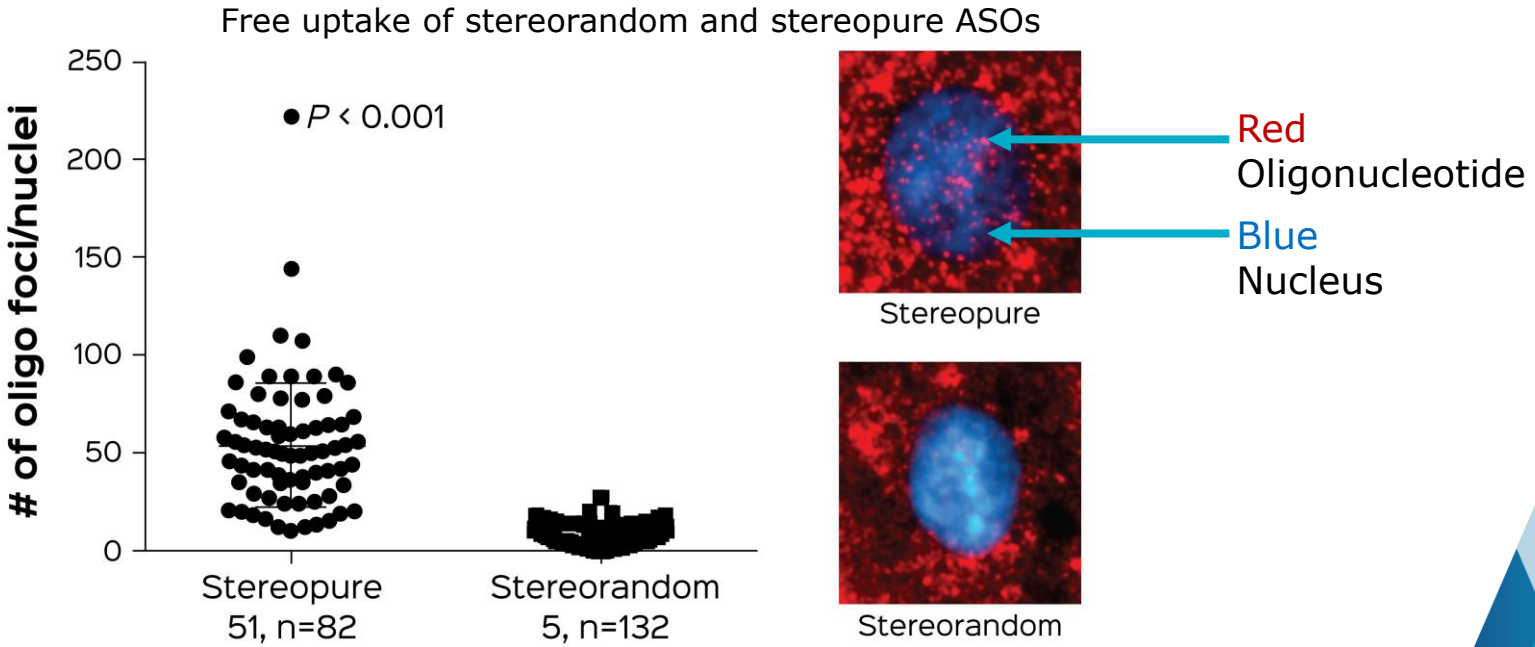


Dystrophin protein restoration *in vitro* was quantified to be between **50-100% of normal** skeletal muscle tissue lysates, as compared to about 1% by drisapersen and eteplirsen analogs

Experimental conditions: DMD protein restoration by Western Blot in patient-derived myotubes with clear dose effect. Free uptake at 10 µM concentration of each compound with no transfection agent.

Exon 51: improved oligonucleotide uptake in the nucleus where splicing occurs

Stereopure oligonucleotides are designed to readily enter the nuclei of cells under free-uptake conditions, which approximates natural delivery in the body



Experimental conditions: Free uptake of ASOs in 18 hour differentiating human DMD myoblasts (Δ48-50).

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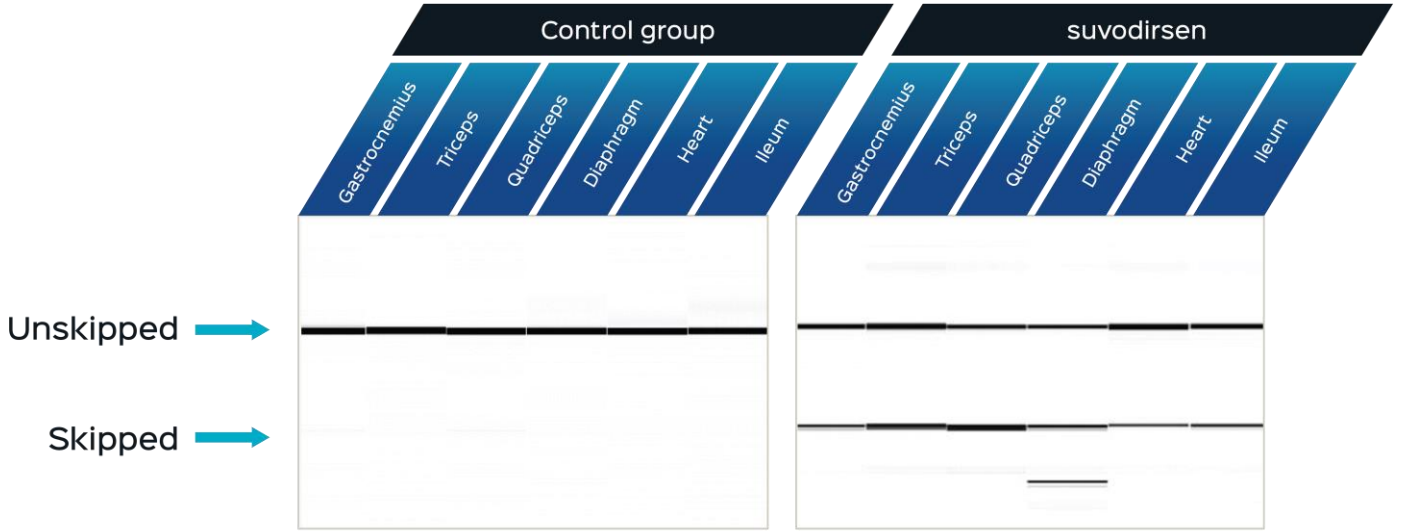
Exon 51: *in vivo* target engagement of suvodirsen in healthy non-human primate

Nested PCR Assay

5 doses @ 30 mg/kg /week for 4 weeks healthy NHP by subcutaneous dosing

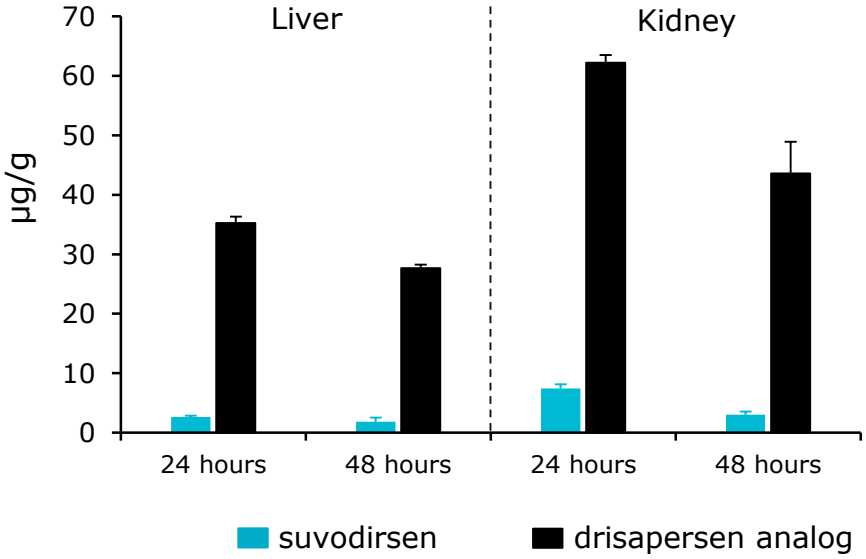


Experimental conditions: Muscle tissues were collected 2 days after the last dose and fresh frozen. Total RNAs were extracted with phenol/chloroform and converted to cDNA using high capacity kit. Nested PCR assay was performed and analyzed by fragment analyzer.

Exon 51: no apparent tissue accumulation observed

- Standard oligonucleotides tend to accumulate in liver and kidney
- Wave rationally designed oligonucleotides optimized to allow compound to clear more effectively
- Suvodirsen demonstrated wide tissue distribution in dose dependent fashion
- No apparent accumulation observed after multiple doses

Single 30-mpk IV injection in *mdx23* mice



Experimental conditions: *Mdx23* mice received a single 30-mg/kg intravenous bolus injection of suvodirsen or drisapersen analog (n=3/group), and sacrificed 24 or 48 hours post dose. Oligo quantifications in tissues were performed using hybridization ELISA assay.

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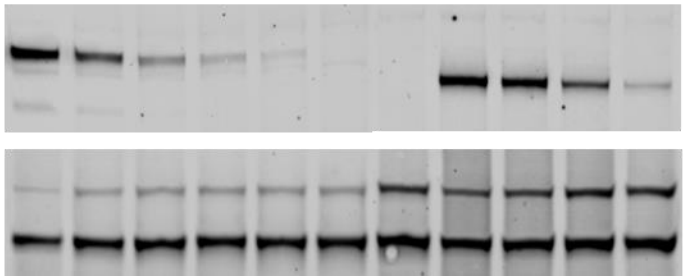
Exon 53: WVE-N531 *in vitro* dose-dependent dystrophin restoration

Dystrophin protein restoration of up to 71%

Western Blot normalized to primary healthy human myoblast lysate

Standard Curve (% WT lysate in D45-52 lysate)						D45-52 Cells					
						Mock	WVE-N531				
						0	10	3.3	1.1	0.3	Conc [uM]
100%	50%	25%	12%	6%	0%	0%	71%	65%	37%	9.5%	% Dystrophin

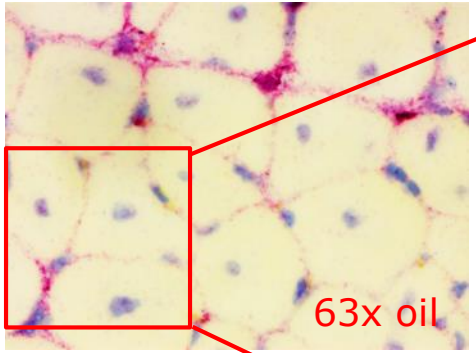


- Free uptake for 6 days in differentiation media with no transfection agent and no peptide conjugated to the oligonucleotide
- Wave stereopure exon 53 candidate demonstrated a dose-dependent increase in dystrophin restoration in DMD patient-derived myoblasts

Topline clinical data expected in H2 2020

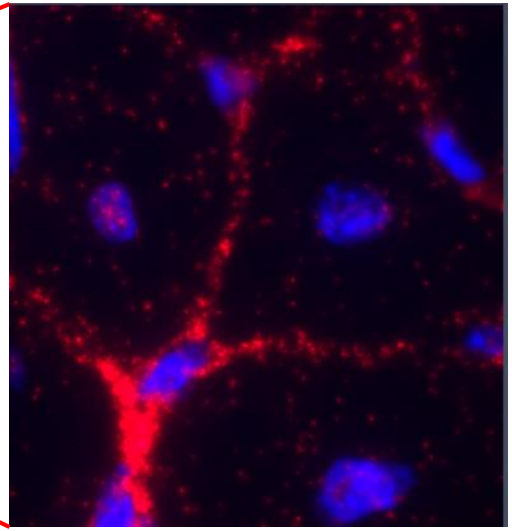
Experimental conditions: D45-52 patient myoblasts were treated with oligonucleotide for 6d under free-uptake conditions in differentiation media. Protein harvested in RIPA buffer and dystrophin restoration analyzed by Western Blot. Signal normalized to vinculin loading control and to primary healthy human myotube lysate (pooled from four donors) forming a standard curve in d45-52 cell lysate.

Exon 53: targeting oligonucleotide rapidly distributes to muscle within 24 hours after injection



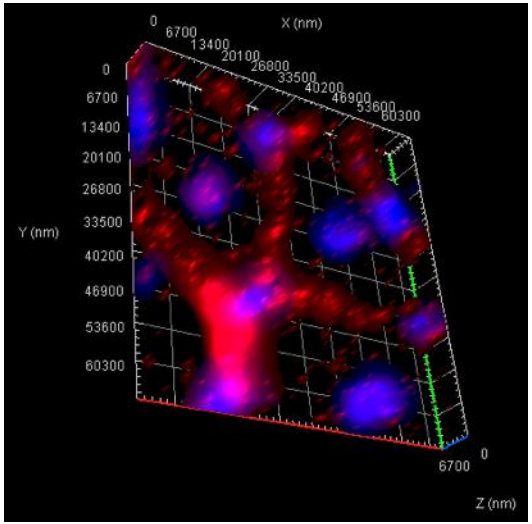
Bright field view

Nucleus: Hematoxylin; Light Blue
Wave oligo: ViewRNA, Fast Red



Fluorescence channel view

Nucleus: Hoechst33342; Blue
Wave oligo: Fast Red/Cy3; Pink Red



Z Stack view

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Data derived from *in vivo* preclinical research.

Experimental conditions: A single dose of stereopure oligonucleotide 30 mg/kg IV was administered to *mdx* 23 mice. Tissues collected 24 hours post dose and ASO was detected in muscles using ViewRNA.

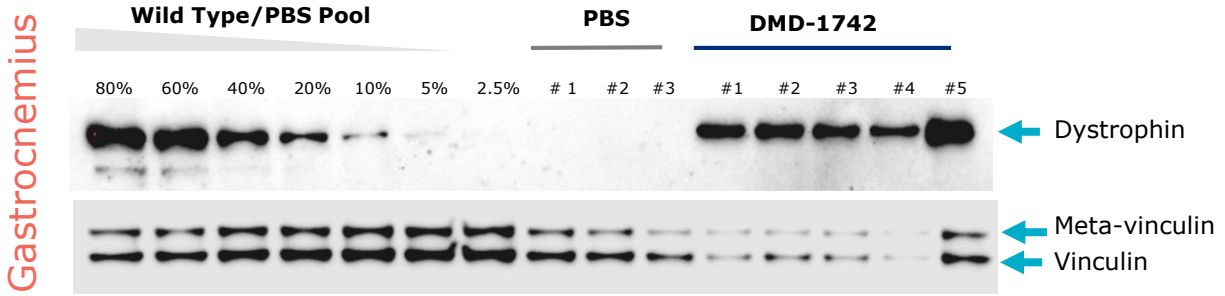
Stereopure surrogate yields substantial dystrophin protein restoration and CK reduction

Multiple Doses (*in vivo mdx23* mice)

Dystrophin Protein Restoration

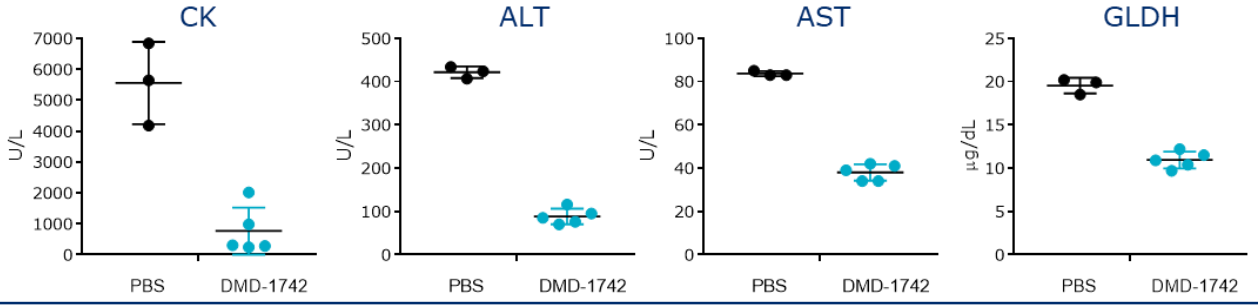
70-90% of dystrophin restoration

DMD-1742 (4 weekly 150-mg/kg IV injections)



Serum Enzyme Levels

87% reduction in creatine kinase (CK) levels



*Numbers indicate individual animals

Note: DMD-1742 is a stereopure oligonucleotide designed to induce exon 23 skipping in the mdx23 mouse model and is a surrogate of suvodirsen, which is designed to induce exon 51 skipping in the human dystrophin transcript

Experimental conditions: Tissues collected 96 hours post final dose. Protein expression determined by Western Blot.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; CK=creatine kinase; GLDH=glutamate dehydrogenase.

Serum and plasma clinical chemistry were measured with an Olympus AU640 (Olympus America) and the manufacturer's reagents and procedures.

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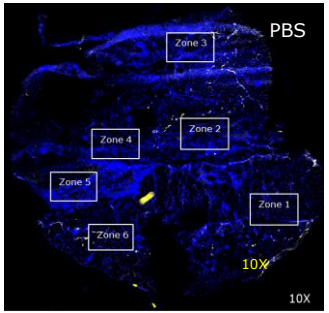
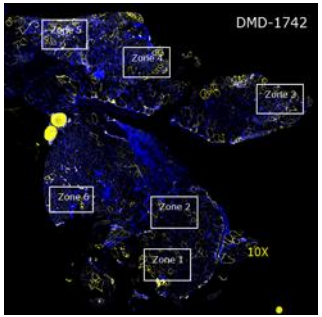
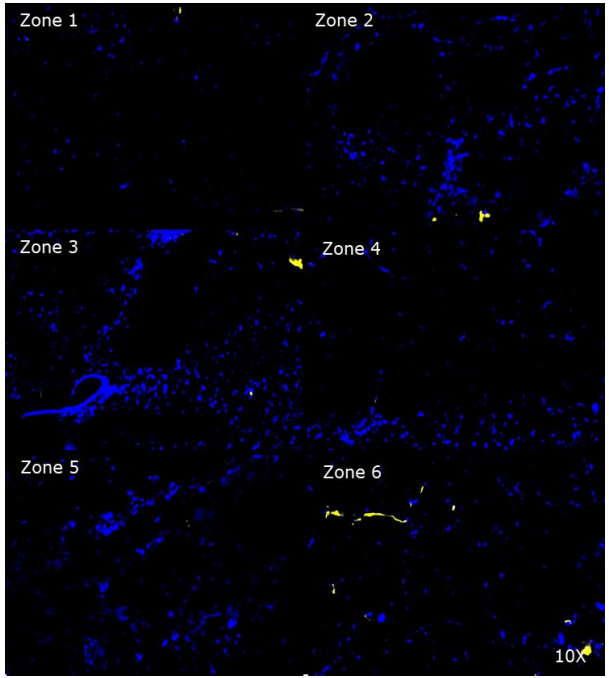
Single dose of surrogate results in restoration of dystrophin in muscle fibers

Immunohistochemistry of dystrophin in gastrocnemius in *mdx23* mice at 4 weeks

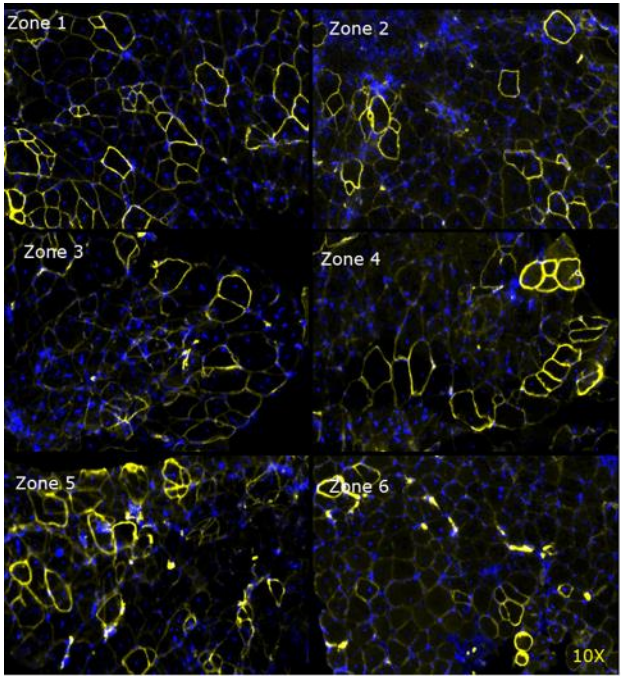




PBS



DMD-1742



Experimental conditions: *mdx23* mice received a single IV injection of PBS or DMD-1742 (150 mg/kg).
Immunohistochemistry: Blue: Nuclei, Hoechest; Yellow: Rabbit anti-Dystrophin(#ab15277) 1:400 diluent, 555/Cy3, Cy3 staining is represented by the yellow color.
10X magnification.

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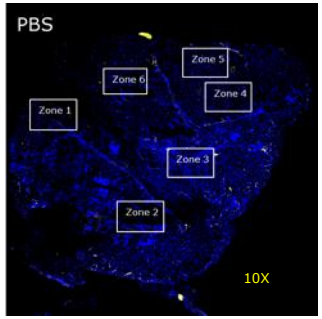
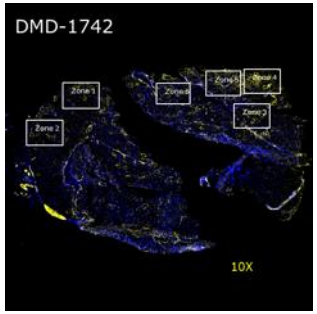
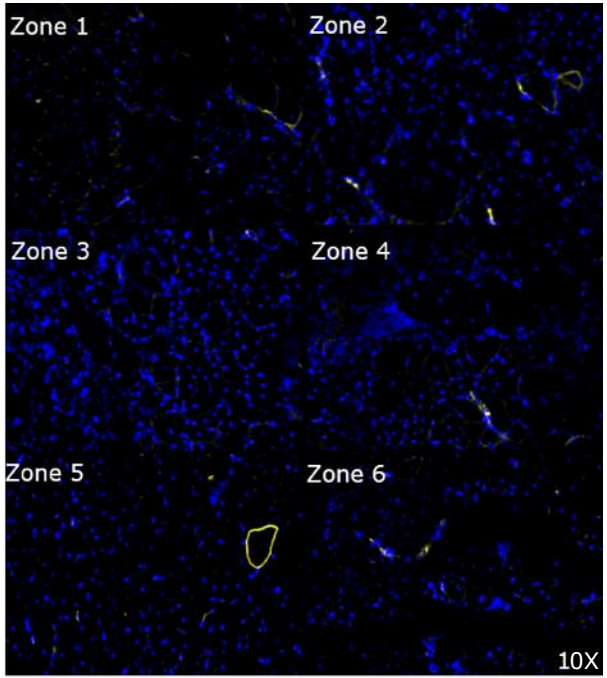
Multiple doses of surrogate result in further restoration of dystrophin in muscle fibers

Immunohistochemistry of dystrophin in gastrocnemius in *mdx23* mice at 4 weeks

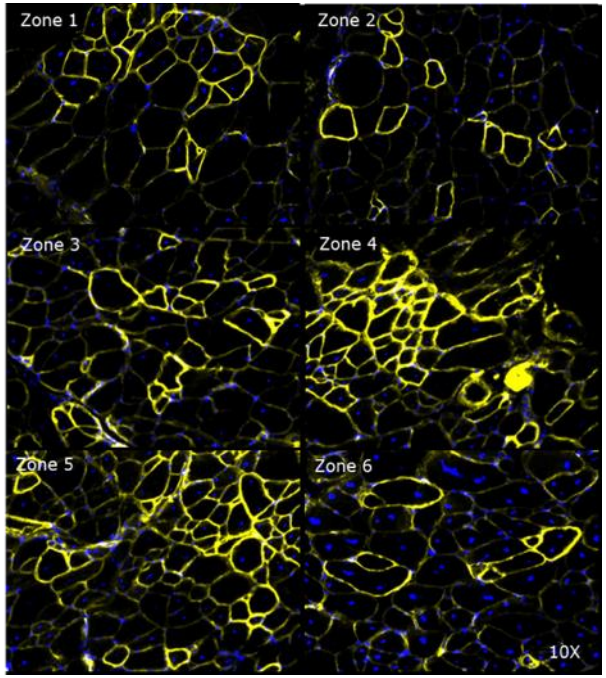




PBS



DMD-1742



Experimental conditions: *mdx23* mice received 4 weekly IV injections of PBS or DMD-1742 (150 mg/kg).
Immunohistochemistry: Blue: Nuclei, Hoechest; Yellow: Rabbit anti-Dystrophin(#ab15277) 1:400 diluent, 555/Cy3, Cy3 staining is represented by the yellow color.
10X magnification.

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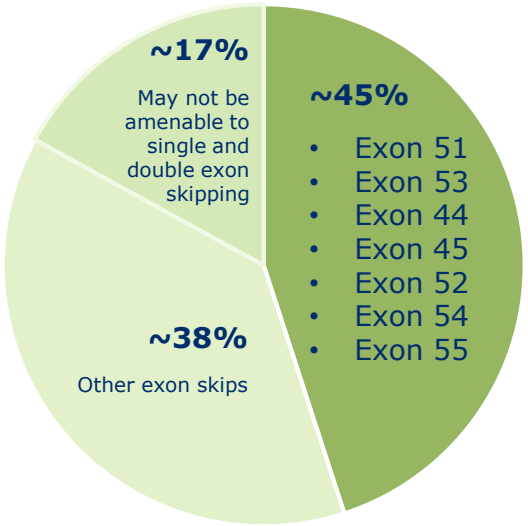
Expansion of stereopure exon skipping DMD portfolio

Percentage of DMD patients amenable to exon skipping therapeutic approach



- Applying learnings from ongoing DMD development efforts and platform advances to explore additional exons for candidate development, including exons 44, 45, 52, 54, 55
- Early leads demonstrate similar *in vitro* exon skipping efficiency as suvodirsen and WVE-N531
- Aim to leverage 21st Century Cures Act to develop additional candidates

Committed to unlocking the promise of genetic medicines to advance the treatment of DMD

Sources: Aartsma-Rus A, et al. *Hum Mutat.* 2009;30:293-299. Bladen CL, et al. *Hum Mutat.* 2015;36:395–402.

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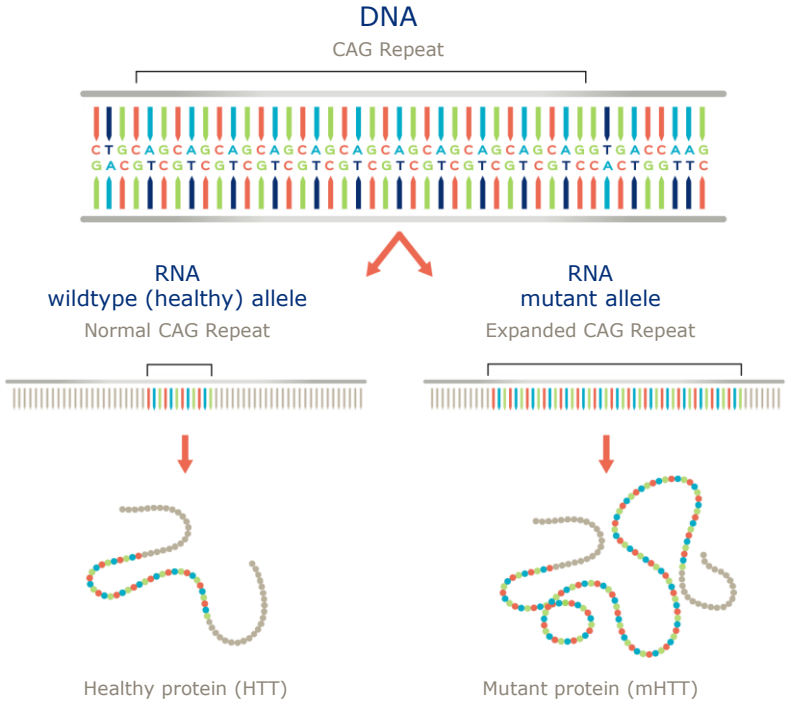
LIFE SCIENCES

Huntington's Disease

Huntington's Disease: a hereditary, fatal disorder

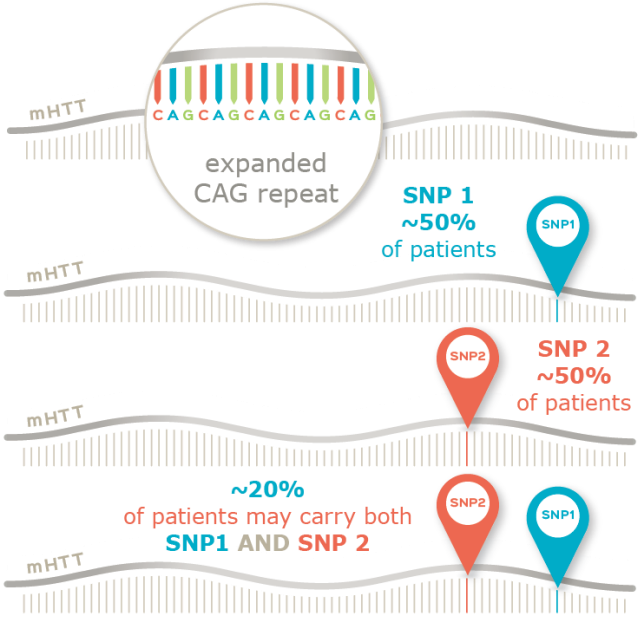
- Autosomal dominant disease, characterized by cognitive decline, psychiatric illness and chorea; fatal
- No approved disease-modifying therapies
- Expanded CAG triplet repeat in HTT gene results in production of mutant huntingtin protein (mHTT); accumulation of mHTT causes progressive loss of neurons in the brain
- Wildtype (healthy) HTT protein critical for neuronal function; suppression may have detrimental long-term consequences
- 30,000 people with Huntington's disease in the US; another 200,000 at risk of developing the condition



Sources: Auerbach W, et al. *Hum Mol Genet.* 2001;10:2515-2523. Dragatsis I, et al. *Nat Genet.* 2000;26:300-306. Leavitt BR, et al. *J Neurochem*. 2006;96:1121-1129. Nasir J, et al. *Cell*. 1995;81:811-823. Reiner A, et al. *J Neurosci.* 2001;21:7608-7619. White JK, et al. *Nat Genet*. 1997;17:404-410. Zeitlin S, et al. *Nat Genet*. 1995;11:155-163. Carroll JB, et al. *Mol Ther.* 2011;19:2178-2185.
Huntington Disease Society of America (HDSA). What is Huntington's disease? Available at: http://hdsa.org/what-is-hd/. Accessed: November 2, 2018.

Wave approach: novel, allele-specific silencing

- Utilize association between single nucleotide polymorphisms (SNPs) and genetic mutations to specifically target errors in genetic disorders, including HD
- Allele-specificity possible by targeting SNPs associated with expanded long CAG repeat in mHTT gene
- Approach aims to lower mHTT transcript while leaving healthy HTT relatively intact
- Potential to provide treatment for up to 70% of HD population (either oligo alone could address approximately 50% of HD population)



Total: Due to overlap, an estimated **~70%** of the total HD patient population carry SNP 1 and/or SNP 2

WAVE LIFE SCIENCES

Source: Kay, et al. Personalized gene silencing therapeutics for Huntington disease. *Clin Genet.* 2014;86:29–36.

Two simultaneous Phase 1b/2a clinical trials

- PRECISION-HD is a global clinical program consisting of the PRECISION-HD1 trial evaluating WVE-120101 targeting SNP1 and the PRECISION-HD2 trial evaluating WVE-120102 targeting SNP2
  - Two parallel, multicenter, double-blind, randomized, placebo-controlled Phase 1b/2a clinical trials for WVE-120101 and WVE-120102, administered intrathecally, with single-ascending dose and multiple-ascending dose portions
  - Primary objective: Assess safety and tolerability of intrathecal doses in early manifest HD patients
  - Key additional objectives: Measurement of total HTT and mHTT; exploratory pharmacokinetic (PK), pharmacodynamic (PD), clinical and MRI endpoints
  - Key inclusion criteria: age ≥25 to ≤65, stage I or II HD who have screened positively for the presence of SNP1 or SNP2
  - Expected to enroll approximately 50 patients per trial
- Open-label extension (OLE) study planned to allow for continued dosing and clinical assessments
  - To include patients previously in the Phase 1b/2a clinical trials
  - Assessments of safety, tolerability, PK, PD, MRI and efficacy using validated clinical outcome measures
- Intend to explore efficacy in early manifest and pre-manifest HD patient populations

Phase 1b/2a readout expected H1 2019

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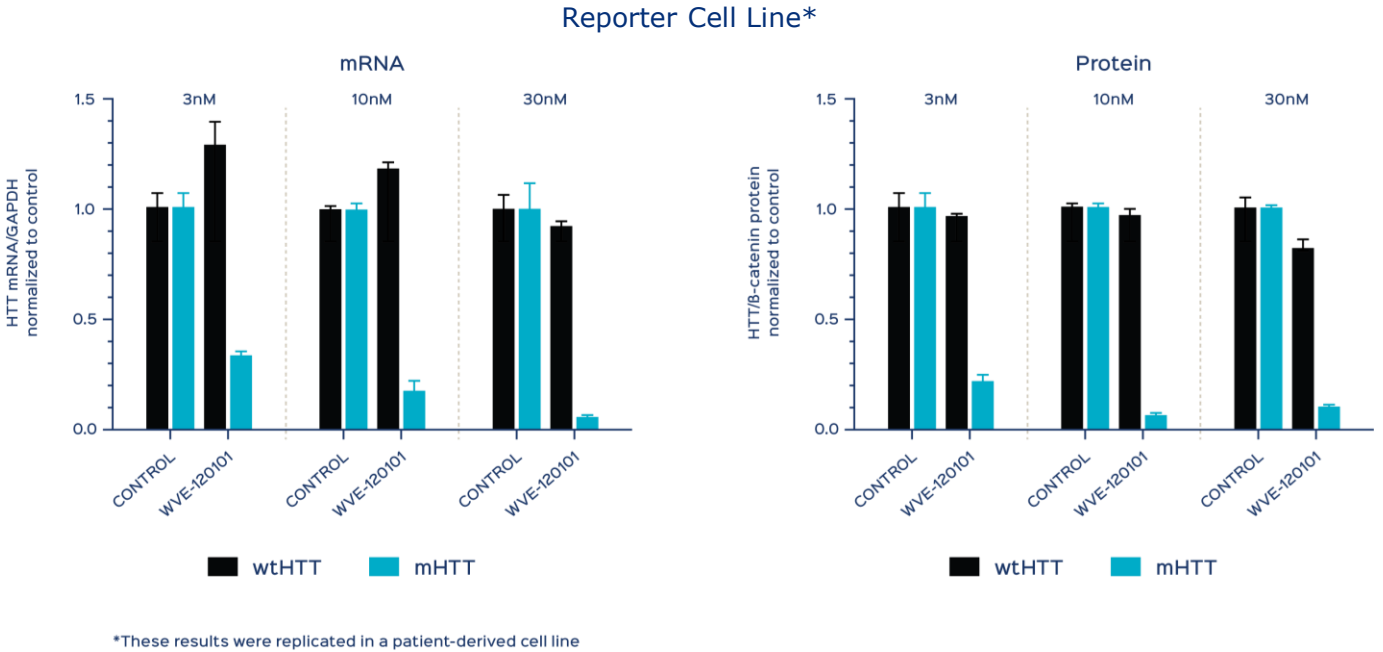
Selective reduction of mHTT mRNA & protein

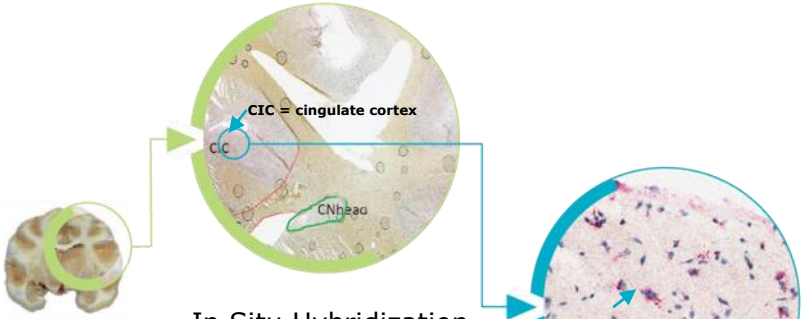


*These results were replicated in a patient-derived cell line

Source: Meena, Zboray L, Svrzikapa N, et al. Selectivity and biodistribution of WVE-120101, a potential antisense oligonucleotide therapy for the treatment of Huntington's disease. Paper presented at: 69th Annual Meeting of the American Academy of Neurology; April 28, 2017; Boston, MA.

Demonstrated delivery to brain tissue

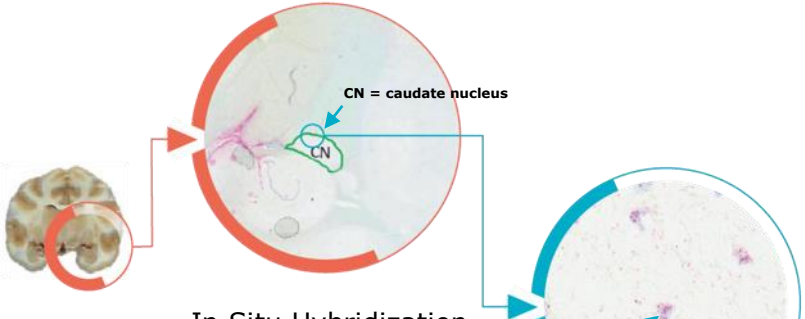
- WVE-120101 and WVE-120102 distribution in cynomolgus non-human primate brain following intrathecal bolus injection



In Situ Hybridization ViewRNA stained tissue

Red dots are WVE-120101 oligonucleotide

Arrow points to nuclear and perinuclear distribution of WVE- 120101 in cingulate cortex



In Situ Hybridization ViewRNA stained tissue

Red dots are WVE-120102 oligonucleotide

Arrow points to nuclear and perinuclear distribution of WVE-120102 in caudate nucleus

Source: Meena, Zboray L, Svrzikapa N, et al. Selectivity and biodistribution of WVE-120101, a potential antisense oligonucleotide therapy for the treatment of Huntington's disease. Paper presented at: 69th Annual Meeting of the American Academy of Neurology; April 28, 2017; Boston, MA.

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LIFE SCIENCES

C9orf72

Amyotrophic Lateral Sclerosis (ALS)

Frontotemporal Dementia (FTD)

C9orf72: a critical genetic risk factor

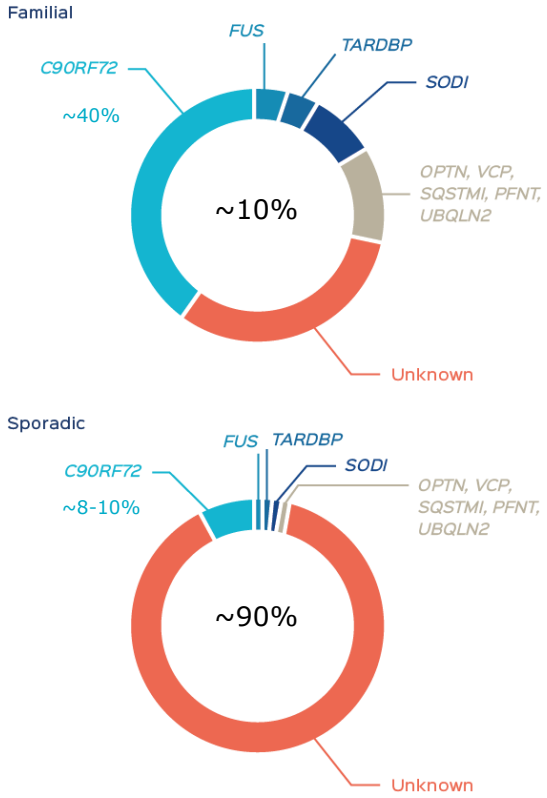
- C9orf72 gene provides instructions for making protein found in various tissues, with abundance in nerve cells in the cerebral cortex and motor neurons
- C9orf72 genetic mutations are the strongest genetic risk factor found to date for the more common, non-inherited (sporadic) forms of Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD); GGGGCC repeat drives the formation and accumulation of dipeptide repeat proteins that accumulate in brain tissue
- First pathogenic mechanism identified to be a genetic link between familial (inherited) ALS and FTD
- Most common mutation identified associated with familial ALS and FTD
- Availability of dipeptide biomarker in CSF has potential to accelerate drug development

Source: DeJesus-Hernandez M, Mackenzie IR, Boeve BF, et al. *Neuron.* 2011;72:245-256. Renton AE, Majounie E, Waite A, et al. *Neuron.* 2011;72:257-268.

Amyotrophic lateral sclerosis

- Fatal neurodegenerative disease characterized by the progressive degeneration of motor neurons in the brain and spinal cord
- Affects approximately 15,000-20,000 people in the US with a median survival of three years
- C9orf72 is present in approximately 40% of familial ALS and 8-10% of sporadic ALS; currently the most common demonstrated mutation related to ALS, far more so than SOD1 or TDP-43
- Pathogenic transcripts of the C9orf72 gene contain hundreds to thousands of hexanucleotide repeats compared to 2-23 in wild-type transcripts; dominant trait with high penetrance

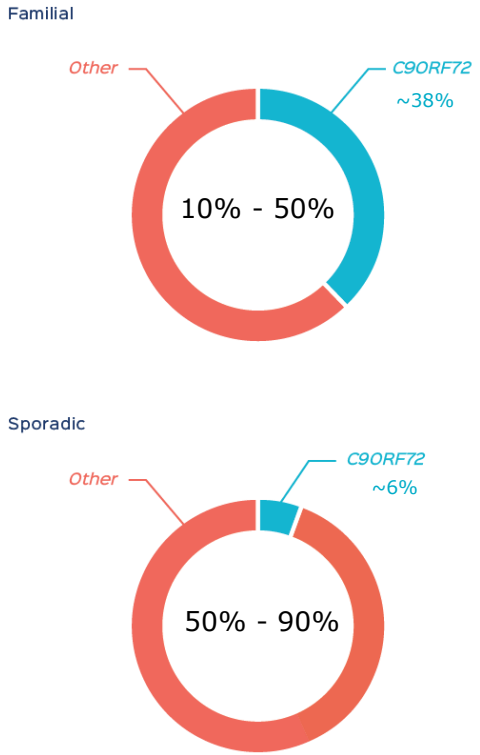
Topline clinical data expected in H2 2020



Source: Renton AE, Chiò A, Traynor BJ. State of play in amyotrophic lateral sclerosis genetics. *Nat Neurosci*. 2014;17:17–23.

Frontotemporal dementia

- Progressive neuronal atrophy with loss in the frontal and temporal cortices characterized by personality and behavioral changes, as well as gradual impairment of language skills
- Affects approximately 55,000 people in the US
- Second most common form of early-onset dementia after Alzheimer's disease in people under the age of 65
- Up to 50% of FTD patients have a family history of dementia, many inheriting FTD as an autosomal dominant trait with high penetrance
- Pathogenic transcripts of the C9orf72 gene contain hundreds to thousands of hexanucleotide repeats compared to 2-23 in wild-type transcripts

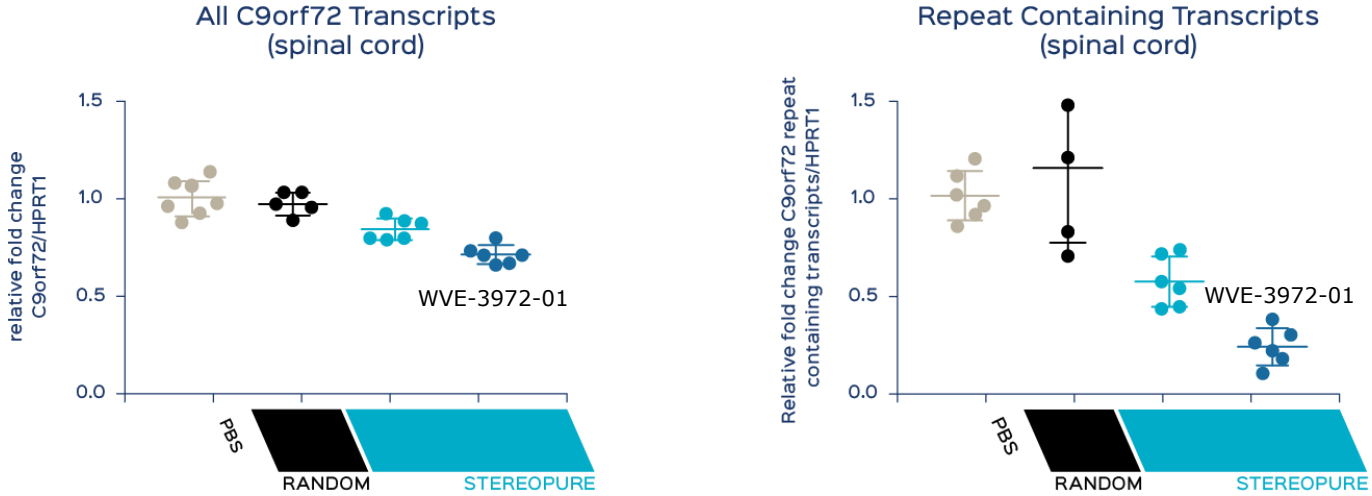


Topline clinical data expected in H2 2020

Sources: Stevens M, et al. Familial aggregation in frontotemporal dementia. *Neurology.* 1998;50:1541-1545. Majounie E, et al. Frequency of the C9orf72 hexanucleotide repeat expansion in patients with amyotrophic lateral sclerosis and frontotemporal dementia: a cross-sectional study. *Lancet Neurol.* 2012;11:323-330.

Selective silencing *in vivo* of expanded C9orf72 repeat transcripts

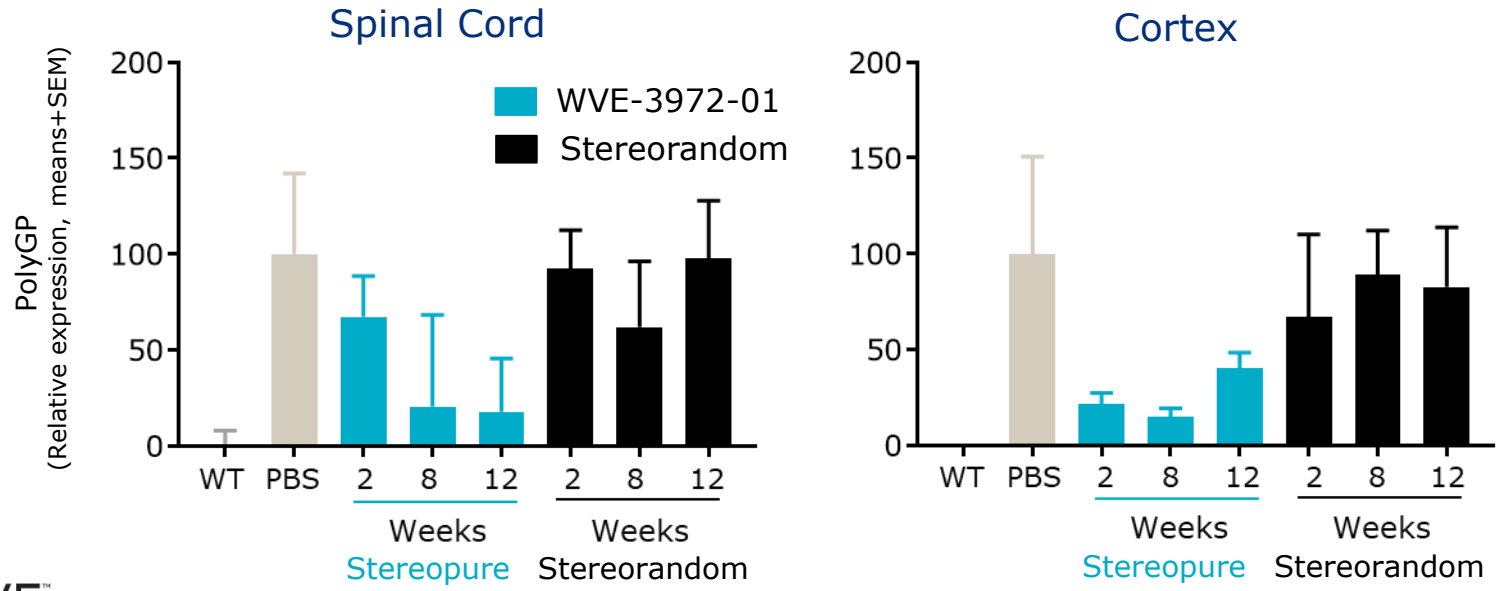
- Wave has developed a series of highly optimized antisense compounds which selectively silence the repeat containing transcript in C9orf72 transgenic mice
- These compounds show target engagement across cell types and regions of the nervous system critically implicated in ALS and FTD



Experimental description: Samples were analyzed using quantitative PCR (Taqman assay)

WVE-3972-01 produces durable reduction in dipeptides *in vivo*

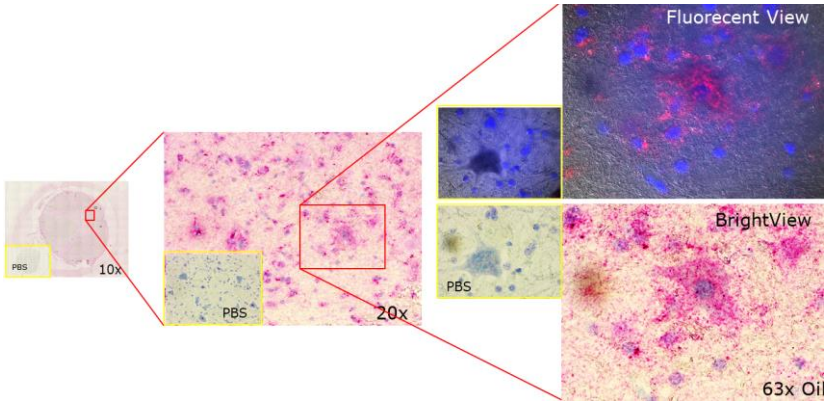
Durable reduction of dipeptide in spinal cord and cortex in C9-BAC mice for at least 12 weeks



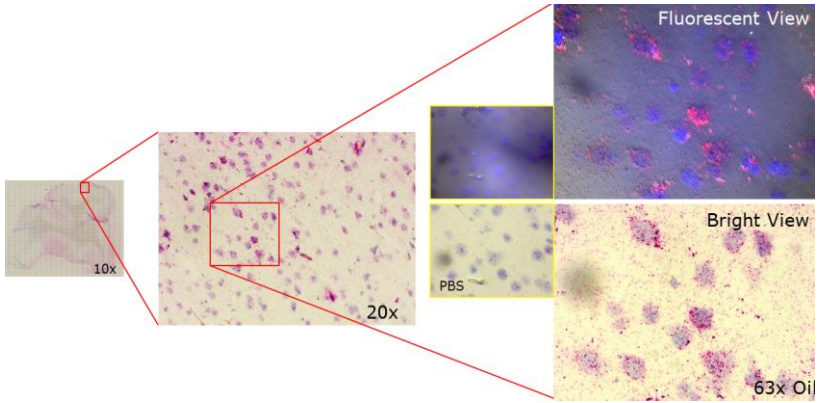
Experimental design: C9-BAC mice received a single ICV injection of PBS or oligonucleotide (100 μg).

WVE-3972-01 in nuclei of neurons in NHP CNS

Spinal cord: Oligonucleotide visualization (ViewRNA) after intrathecal delivery in NHPs



Frontal Cortex: Oligonucleotide visualization (ViewRNA) after intrathecal delivery in NHPs



Blue: Nuclear, Hematoxylin; Pink Red: ASO/ViewRNA, Fast Red/Cy3

Widespread and sustained distribution in nuclei of neurons in spinal cord and frontal cortex

NHP = non-human primate.
Experimental design: Cynomolgus monkeys were administered 3 weekly IT doses of ASO; tissues were collected 48 hours after last injection.

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Ophthalmology

Building a portfolio for inherited retinal diseases

Inherited retinal diseases (IRDs)

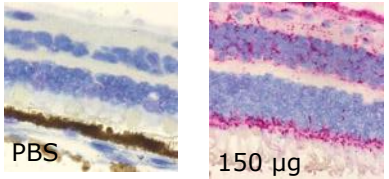
- Rare eye disorders caused by genetic mutations leading to progressive vision loss
- No approved therapies for almost any IRDs
- Approximately 200,000 affected in the U.S. and millions world-wide

Wave opportunity

- Oligonucleotides allow for intravitreal (IVT) injection; targeting twice per year dosing
- Stereopure oligonucleotides open up novel strategies in both dominant and recessive IRDs; potential for potent and durable effect with low immune response
- Established imaging markers, easily identifiable patient population and historical ophthalmology trial success rates suggest clear path to market

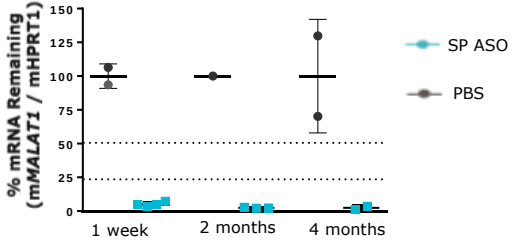
Single IVT injection of stereopure oligonucleotide to NHP results in distribution throughout all layers of the retina and potent, extended duration of effect

Broad Distribution
One Week Post-Dose



MALAT1 oligonucleotide detected using ViewRNA assay; pink = oligonucleotide

>95% Knockdown
in Retina Tissue



Genetic target	Inherited retinal disease	US Population Addressable by Wave Approach
RHO P23H	Retinitis pigmentosa	~1,800
USH2A	Usher syndrome 2A	~5,000
ABCA4	Stargardt disease	~2,000
CEP290	Leber congenital amaurosis 10	~1,000

Initial candidate expected in H2 2019

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Sources: Daiger S, et al. *Clin Genet*. 2013;84:132-141. Wong CH, et al. *Biostatistics.* 2018; DOI: 10.1093/biostatistics/kxx069. Athanasiou D, et al. *Prog Retin Eye Res.* 2018;62:1–23. Daiger S, et al. *Cold Spring Harb Perspect Med.* 2015;5:a017129. Verbakel S, et al. *Prog Retin Eye Res.* 2018:66:157-186.

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Partnerships

Collaborating to maximize portfolio and platform

Takeda

- **$230+ million** in committed cash; eligible for milestones and royalties in excess of $2 billion*
- Takeda option on **global 50:50 share** of CNS programs in HD, ALS, FTD and SCA3
- **Fully funded CNS R&D** with Takeda right to license additional preclinical CNS targets over four years

Pfizer

- **$40 million** upfront payment; **$871 million** in potential milestone payments and royalties
- **Advancing 5 targets**, including APOC3, for the treatment of metabolic liver diseases
- Leveraging **Wave proprietary chemistry platform** across modalities with GalNAc and Pfizer's hepatic targeting technology

Platform technologies

deep genomics

- Applying **artificial intelligence** to discover novel therapies for genetic neuromuscular disorders

READCOOR

- Utilizing **3D imaging** to assess target engagement in specific regions, cell types and subcellular compartments of the brain

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*Assuming Takeda advances six programs that achieve regulatory approval and commercial sales, Wave will be eligible to receive up to $2 billion in cash milestone payments, of which more than $1 billion would be in precommercial milestone payments.

Upcoming Wave catalysts

- **H1 2019: Data expected in HD from Phase 1b/2a trials for WVE-120101 and WVE-120102**
  - Potential to be first two allele-specific disease-modifying therapies selectively lowering mHTT
- **2019: Initiate Phase 2/3 clinical trial for suvodirsen (WVE-210201) in DMD**
  - Protocol selected for FDA complex innovative trial designs (CID) pilot program
- **H2 2019: Interim dystrophin data readout expected in DMD for suvodirsen (WVE-210201)**
- **H2 2019: Initial development candidate for inherited retinal disease**
- **H2 2020:**
  - Anticipate filing an NDA and pursuing accelerated approval for suvodirsen (WVE-210201) in exon 51 amenable DMD
  - Topline clinical data expected in DMD for WVE-N531 targeting exon 53
  - Topline clinical data expected from WVE-3972-01 C9orf72 programs

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Realizing the potential of genetic medicines

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