



WAVE[™]
LIFE SCIENCES

Wave Life Sciences
Corporate Presentation
June 5, 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.

Targeting genetically defined diseases with stereopure oligonucleotides

Building fully integrated genetic medicines company led by neurology development programs

Neuromuscular

- **Lead clinical program: Suvodirsen Phase 2/3 trial initiation expected in July 2019 for DMD (exon 51); program on development path toward US and global approvals**
- Advancing additional exon skipping candidates for DMD
- Commercialization activities underway

100% global rights

CNS

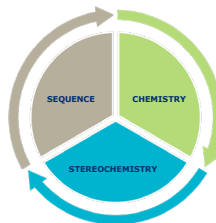
- **Lead clinical program: Two Phase 1b/2a trials ongoing for Huntington's disease using differentiated allele-selective approach**
- Advancing C9orf72 candidate for ALS and FTD
- SNP3 (HD) and ATXN3 (SCA3)

Takeda 50:50 option

Ophthalmology

- Initial candidate selection ongoing for inherited retinal diseases

100% global rights

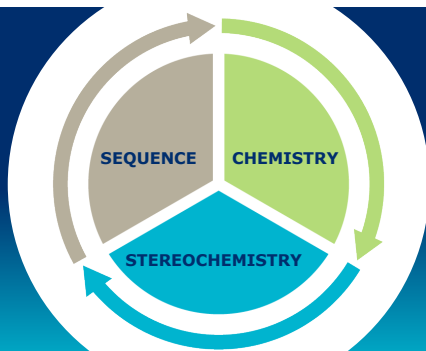




Enables Wave to target genetically defined diseases with stereopure oligonucleotides across multiple therapeutic modalities

DESIGN

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

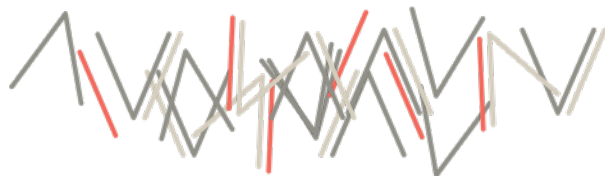


OPTIMIZE

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

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



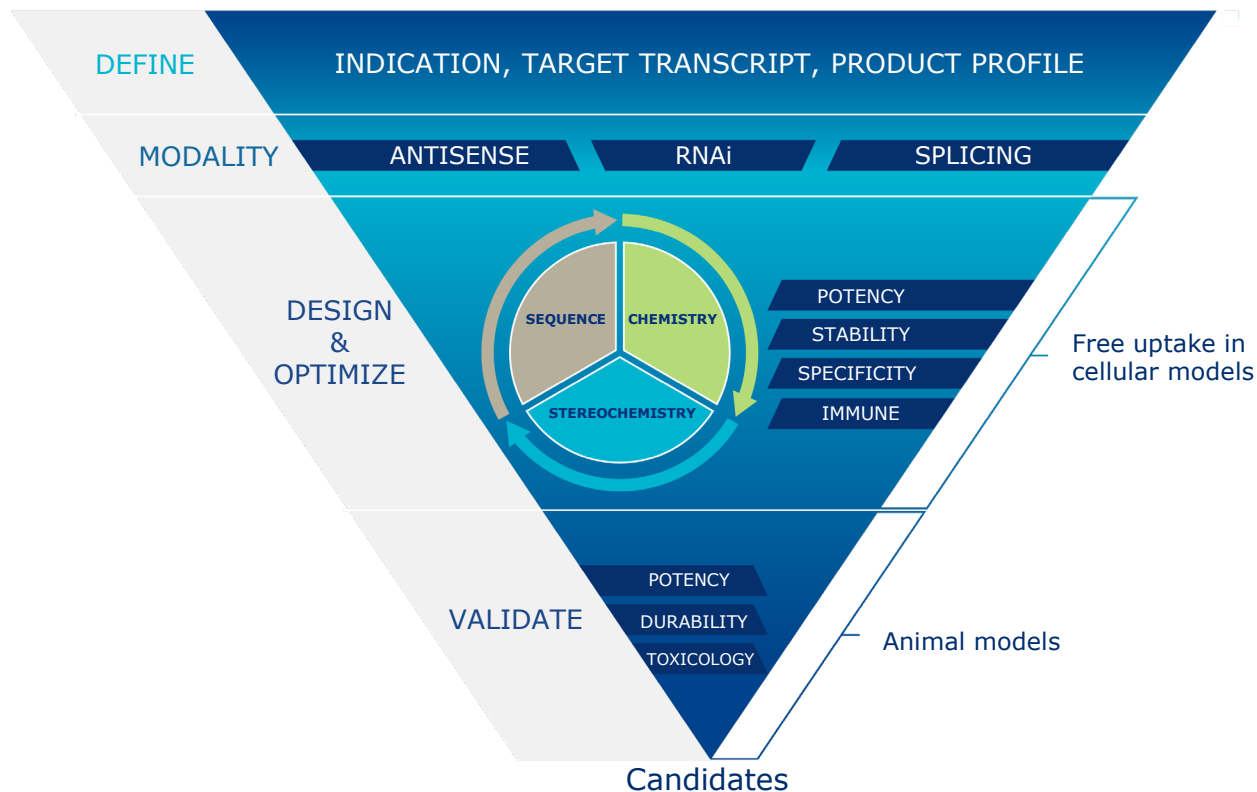
WAVE RATIONAL DESIGN

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

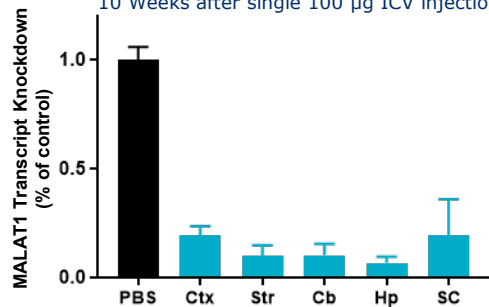
Creating a new class of oligonucleotides



Optimizing potency and durability across multiple tissues

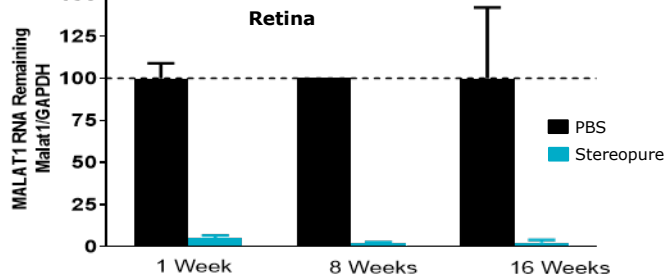
CNS

MALAT1 Transcript Knockdown in Mice
10 Weeks after single 100 µg ICV injection



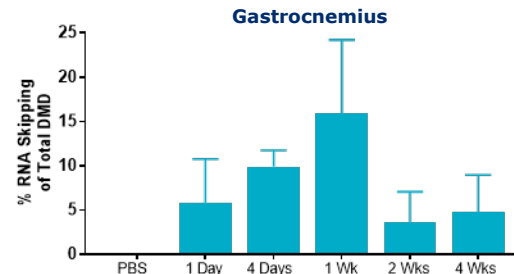
Eye

MALAT1 Knockdown in Non-Human Primates
Single 450 µg IVT injection



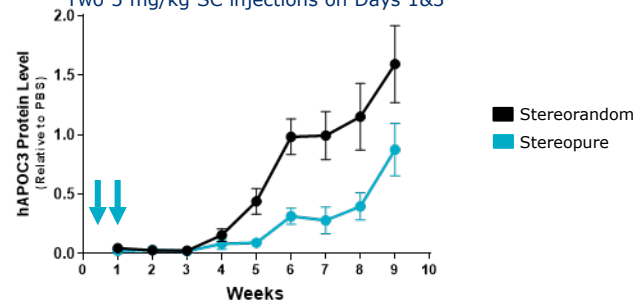
Muscle

DMD: Percent Skipped Transcript in *mdx23* Mice
Single 150 mg/kg IV injection



Liver

Knockdown of Serum hAPOC3 Protein Levels in Mice
Two 5 mg/kg SC injections on Days 1&3

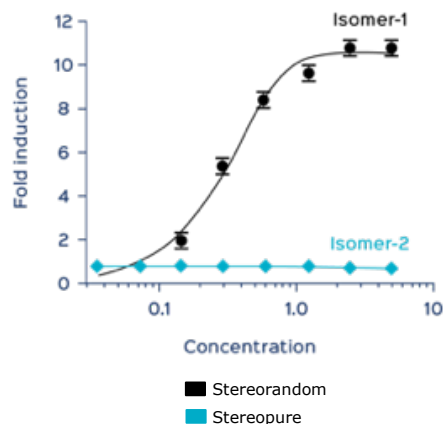


Data represented in this slide from *in vivo* studies. CNS: PBS = phosphate buffered saline; Ctx = cortex; Str = striatum; Cb = cerebellum; Hp = hippocampus; SC = spinal cord. ICV = intracerebral; IVT = intravitreal; IV = intravenous; SC = subcutaneous.

Stereochemistry affects immune activation

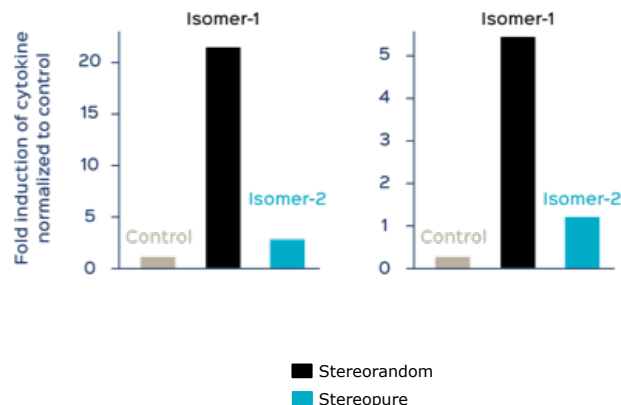
Human TLR9 Activation

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



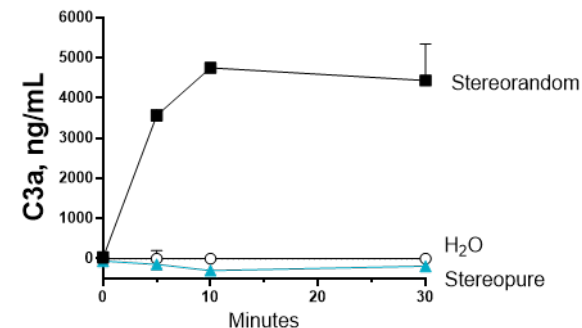
Cytokine Induction

Cytokine induction in human PBMC assay



Complement Activation

Complement activation in non-human primate serum assay



Pipeline spanning multiple modalities, novel targets

THERAPEUTIC AREA/MODALITY	TARGET	DISCOVERY	CANDIDATE	CLINICAL	REGISTRATION	ESTIMATED U.S. PREVALENCE*	PARTNER
MUSCLE							
Duchenne muscular dystrophy Exon-skipping	Suvodirsen Exon 51	OLE and planned Phase 2/3			U.S. A.A. filing planned in 2H 2020 pending dystrophin data	~2,000	
	WVE-N531 Exon 53					~1,250	
	Exons 44, 45, 52, 54, 55					~3,000	
Neuromuscular diseases	Multiple						
CNS							
Huntington's disease Allele – selective silencing	WVE-120101 mHTT SNP1	Phase 1b/2a				~10,000 / ~35,000	Takeda 50:50 option
	WVE-120102 mHTT SNP2	Phase 1b/2a				~10,000 / ~35,000	Takeda 50:50 option
	mHTT SNP3					~8,000 / ~30,000	Takeda 50:50 option
ALS and FTD Allele – selective silencing	WVE-C092 C9orf72					~1,800 (ALS) ~7,000 (FTD)	Takeda 50:50 option
Spinocerebellar ataxia 3 Silencing	ATXN3					~4,500	Takeda 50:50 option
CNS diseases	Multiple†						Takeda milestones & royalties
OPHTHALMOLOGY							
Retinal diseases	Multiple						
HEPATIC							
Metabolic liver diseases Silencing	Multiple						Pfizer milestones & royalties

Suvodirsen
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



Potential benefits of stereopure oligonucleotide approach to treating Duchenne muscular dystrophy

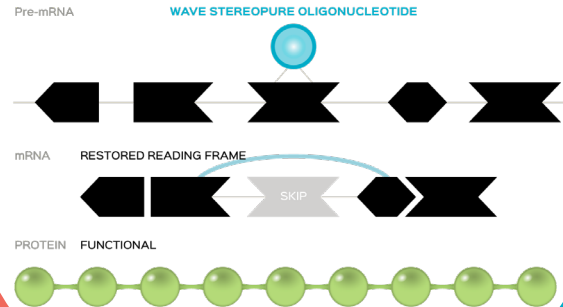
Delivery

- Entry into cells (including progenitor cells) via free-uptake
- Enhanced nuclear uptake

Repeat administration

- Repeat administration may better address muscle cell turnover and need for broad distribution

Exon skipping



Functional dystrophin

- Production of meaningful levels of functional dystrophin protein
- Expected to result in therapeutic benefit

Scalable manufacturing

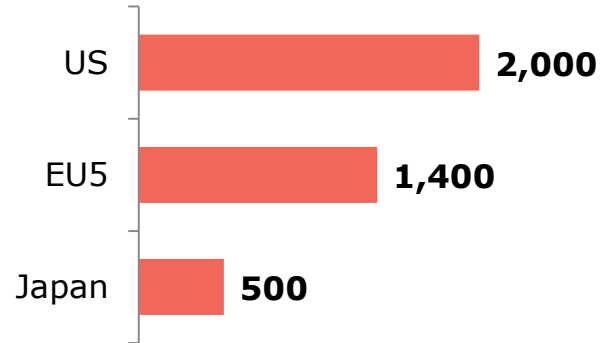
- Scalable manufacturing process to meet clinical and commercial supply requirements
- Cost of goods consistent with conventional oligonucleotide therapies

Suvodirsen: Wave's lead stereopure exon skipping oligonucleotide for exon 51 amenable DMD

Exon 51: Most frequent mutation among DMD patients

- ~13% of DMD patients amenable to Exon 51 skipping
- One exon-skipping therapy conditionally approved by FDA
 - Minimal increase in dystrophin expression over baseline observed after 48 weeks; **Mean increase 0.28%, Median increase 0.1%**¹
 - Clinical benefit not established
 - Not approved ex-US
- Demand for additional treatment options remains high
- Established US and EU regulatory paths

Prevalent patient populations amenable to exon 51 skipping²

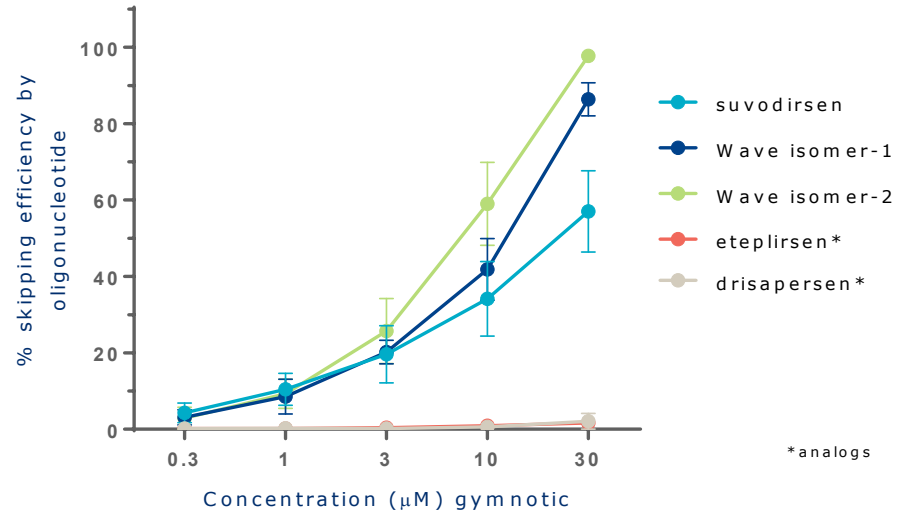


Prevalent patient population represents **>\$1.5B** global market opportunity³

Exon 51: improved skipping efficiency

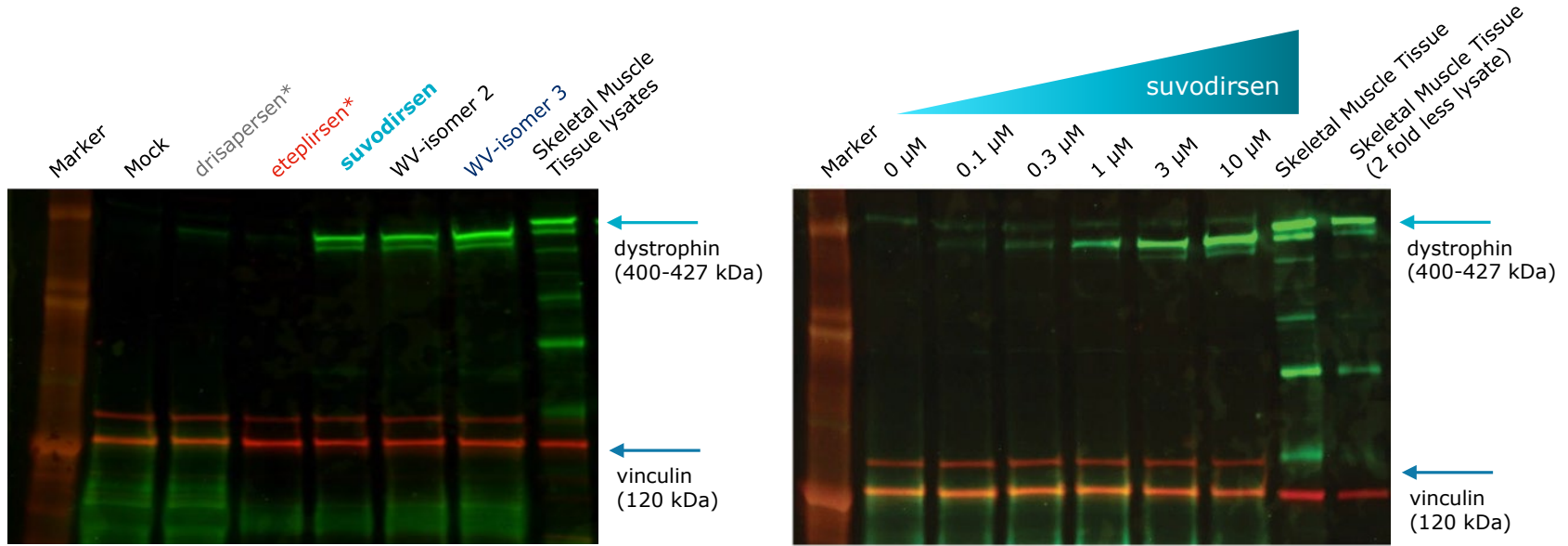
- RNA skipping determined by quantitative RT-PCR
- Wave isomers demonstrated a dose-dependent increase in skipping efficiency *in vitro*
- Free uptake at 10uM concentration of each compound with no transfection agent
- Same foundational stereopure chemistry for Wave isomers; individually optimized to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

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



*analogs

Exon 51: increased dystrophin restoration *in vitro*



*Analog

Oligonucleotide at 10 µM concentration

suvodirsen

drisapersen analogue

eteplirsen analogue

In vitro dystrophin restoration

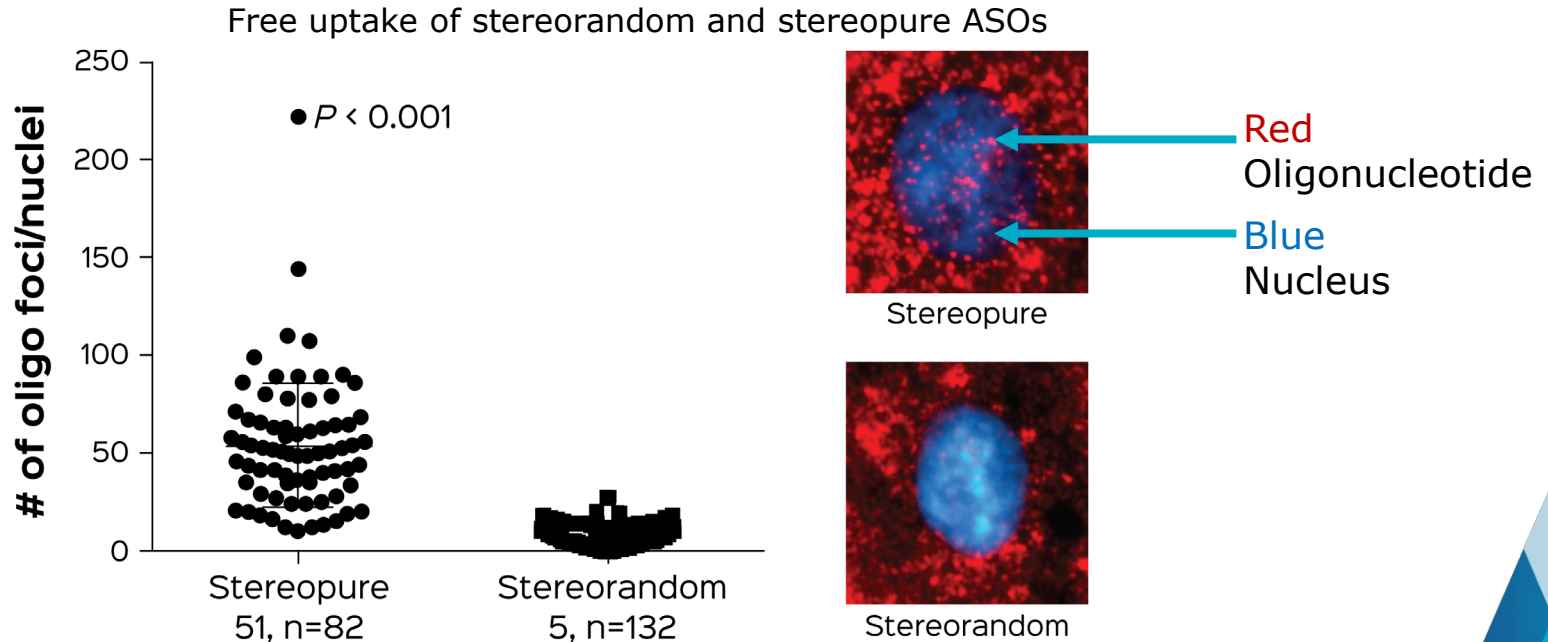
~52%

~1%

~1%

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

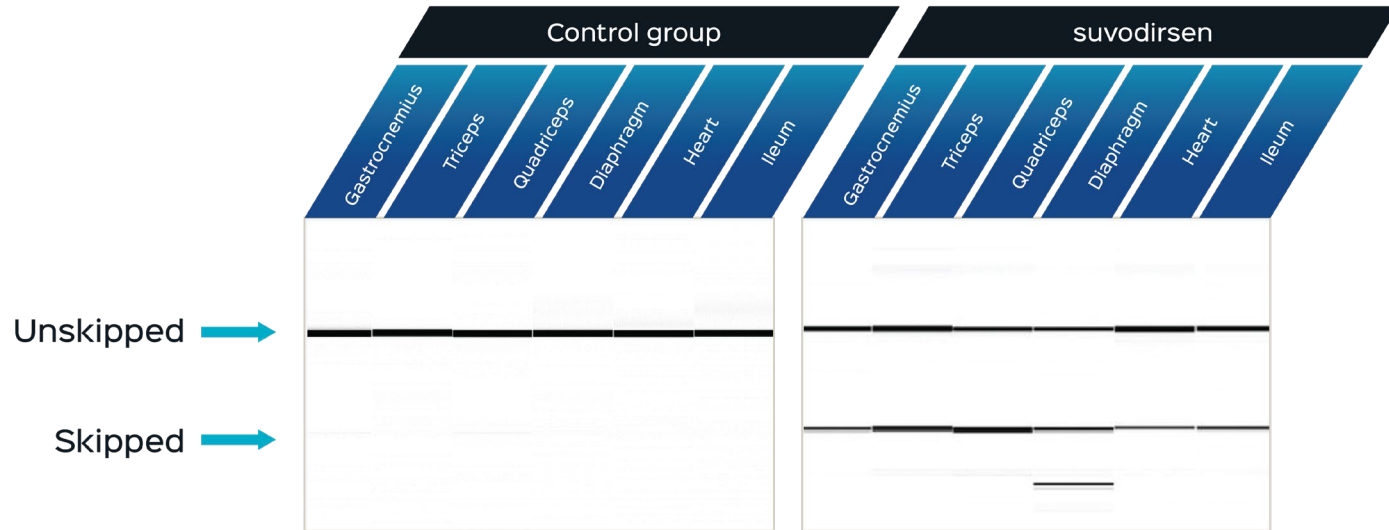
Stereopure oligonucleotides are designed to readily enter the nuclei of cells under free-uptake conditions, which approximates natural delivery in the body



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

Nested PCR Assay

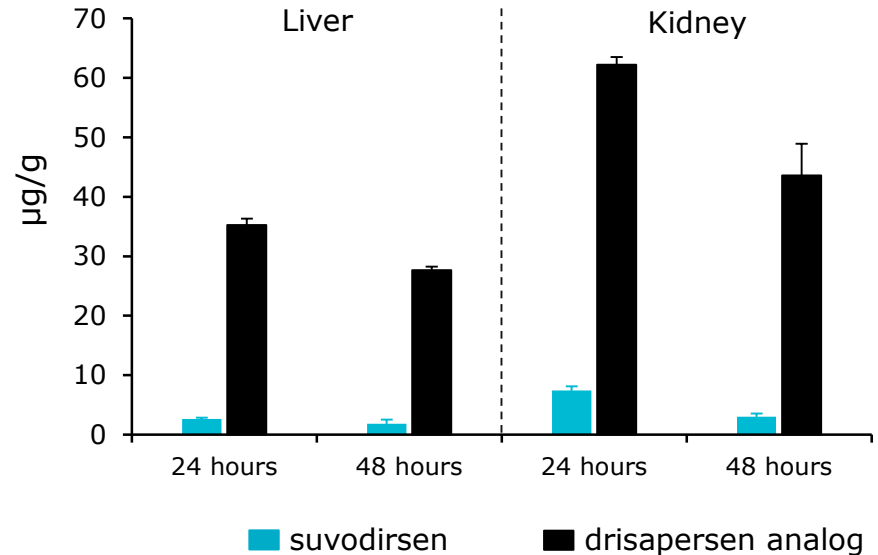
5 doses @ 30 mg/kg /week for 4 weeks healthy NHP by subcutaneous dosing



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 broad tissue distribution in dose dependent fashion
- No apparent accumulation observed after multiple doses

Single 30-mpk IV injection in *mdx23* mice



Suvodirsen: Phase 1 and OLE clinical trials

Phase 1 Single Ascending Dose Trial

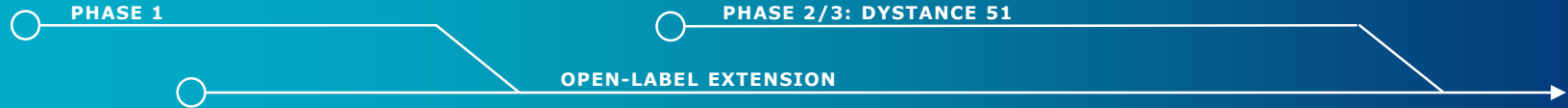
- 40 DMD patients amenable to exon 51 skipping¹
- ~20% of patients had received eteplirsen previously (following wash out)

Suvodirsen had a favorable safety and tolerability profile in context of available treatments for continued development in OLE and Phase 2/3 trial

Open-Label Extension Trial *Ongoing*

- Open to all patients in Phase 1 trial
- 1:1 randomization to 5 mg/kg and 3.5 mg/kg doses
- Patients receiving weekly IV doses of suvodirsen
- Interim analysis of dystrophin expression expected in 2H 2019

Suvodirsen: Path towards US and global approvals



Phase 1

- Phase 1 single ascending dose clinical trial
- Based on *in vitro* and *in vivo* preclinical studies and Phase 1 clinical results, two suvodirsen doses selected for Phase 2/3 clinical trial
- **Study complete**

Open-label extension (OLE)

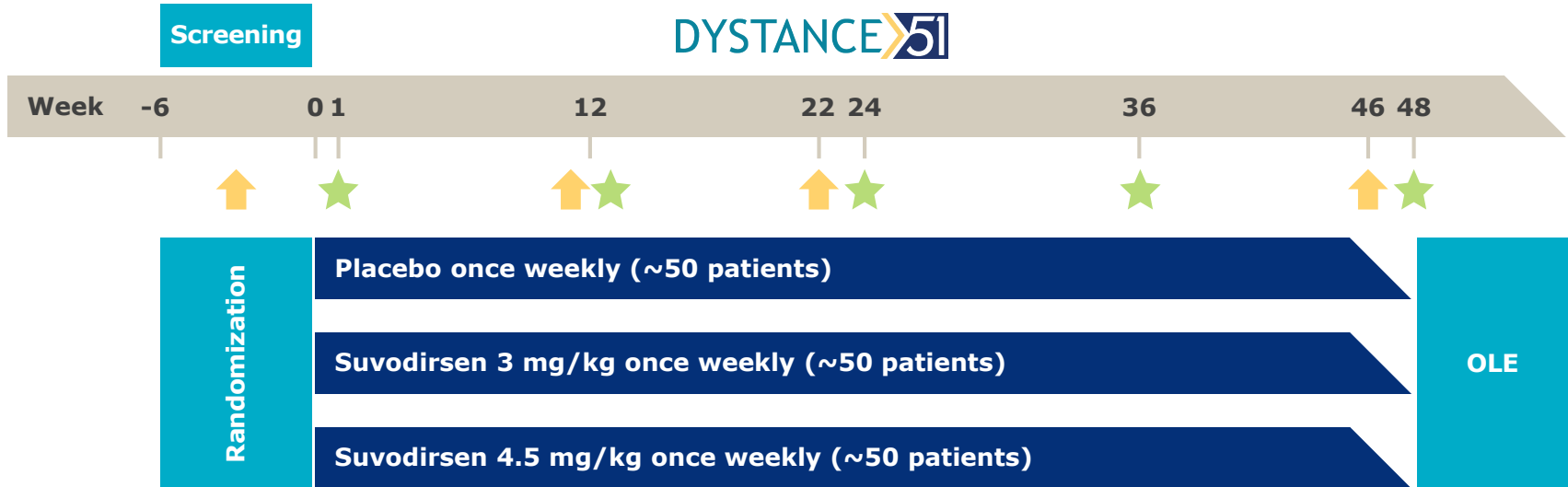
- Multi-dose, open-label study with patients from Phase 1 clinical trial currently underway
- Data will be an important component of submission for accelerated approval in US
- **On track to deliver interim analysis of dystrophin expression in 2H 2019**

Phase 2/3 DYSTANCE 51

- Phase 2/3 clinical trial to assess clinical efficacy and dystrophin expression
- Efficacy and safety data to serve as basis of regulatory submissions globally
- **Expect to initiate in July 2019**

2H 2020: Potential FDA accelerated approval filing in exon 51 amenable DMD

Phase 2/3 study selected for FDA Complex Innovative Trial Design (CID) pilot program



- Designed with input from global regulatory communities and DMD patient community
- DMD historical control data will be leveraged to help reduce number of patients required to deliver conclusive clinical efficacy results and potentially accelerate study completion

Building a portfolio to transform the care of DMD

Suvodirsen targeting exon 51

- Phase 2/3 trial expected to initiate in July 2019 for global regulatory submissions
- Potential FDA accelerated approval filing in 2H 2020, pending positive clinical dystrophin expression data

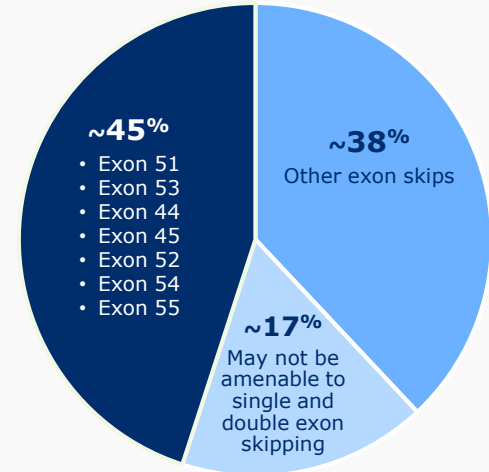
WVE-N531 targeting exon 53

- Topline clinical data expected in 2H 2020

Advancing candidate development for exons 44, 45, 52, 54, 55

- Early leads demonstrated similar *in vitro* exon skipping efficiency as suvodirsen and WVE-N531

Percentage of patients with DMD amenable to exon skipping therapeutic approach

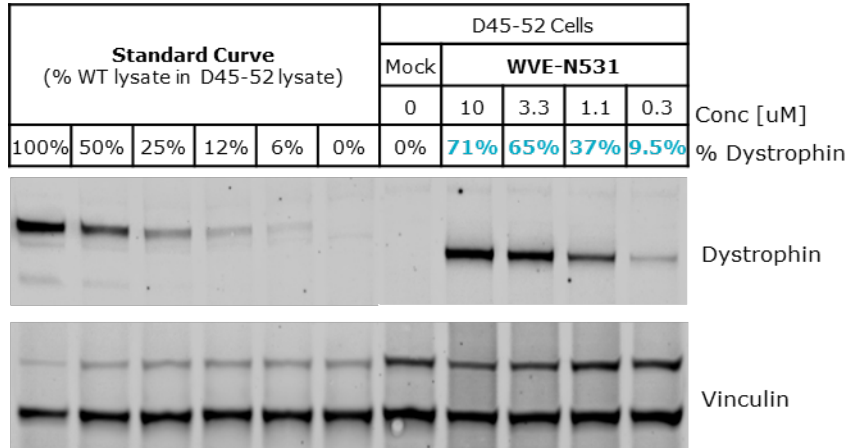


Initiating commercialization activities in anticipation of first potential launch in US

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

Dystrophin protein restoration of up to 71%

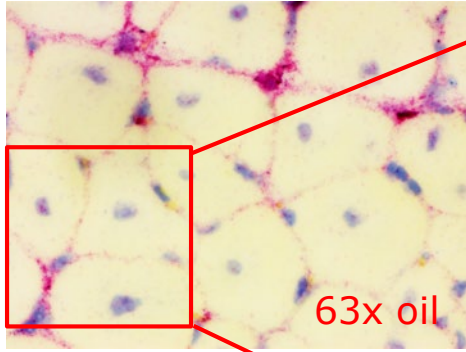
**Western Blot normalized to
primary healthy human myoblast lysate**



- 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 2H 2020

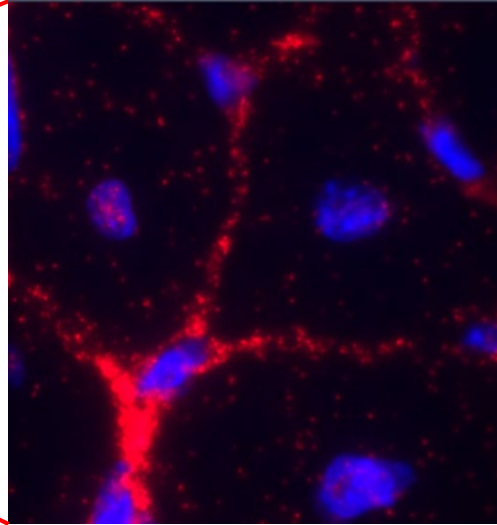
Exon 53: targeting oligonucleotide rapidly distributes to muscle within 24 hours after injection



Bright field view

Nucleus: Hematoxylin; Light Blue

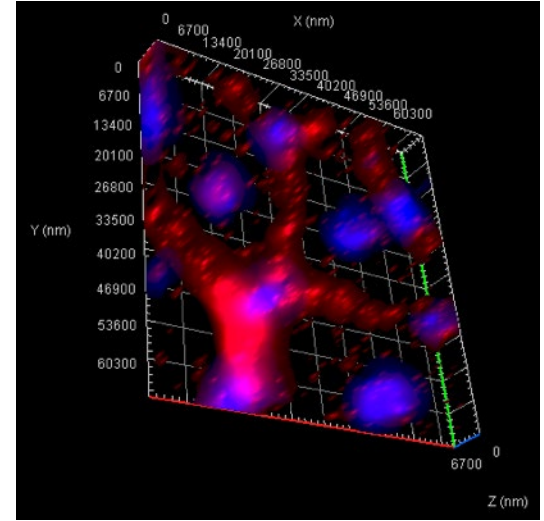
Wave oligo: ViewRNA, Fast Red



Fluorescence channel view

Nucleus: Hoechst33342; Blue

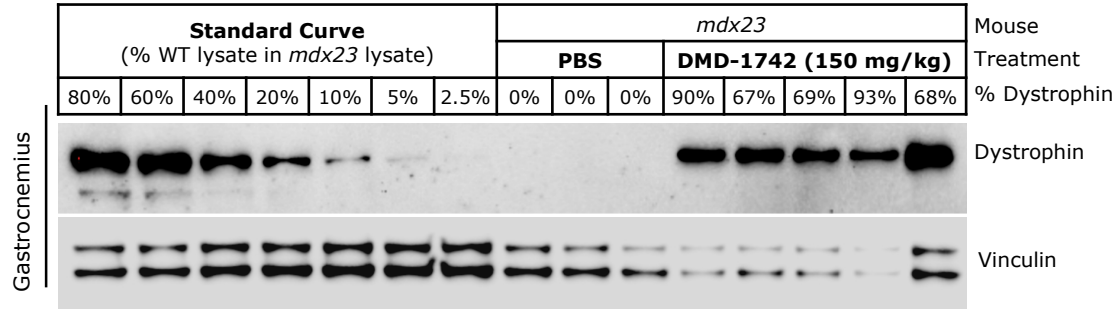
Wave oligo: Fast Red/Cy3; Pink Red



Z Stack view

In vivo mdx23 dystrophin protein with oligonucleotides

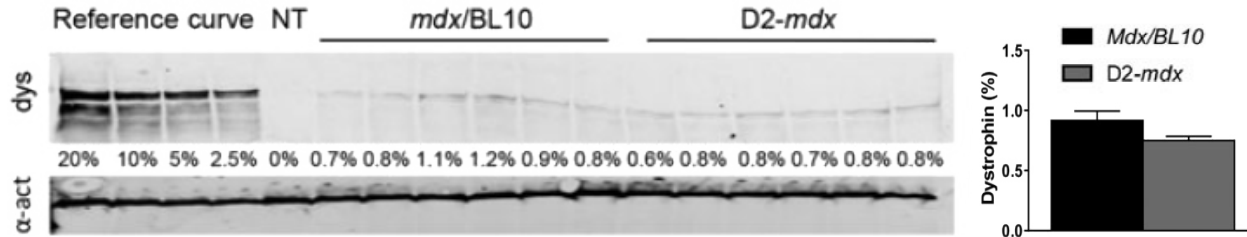
***In vivo* dystrophin protein restoration (stereopure surrogate, 150 mg/kg, 4 weekly IV doses)**



- 70 – 90% dystrophin restoration
- 87% reduction in creatine kinase (CK) levels

Published literature

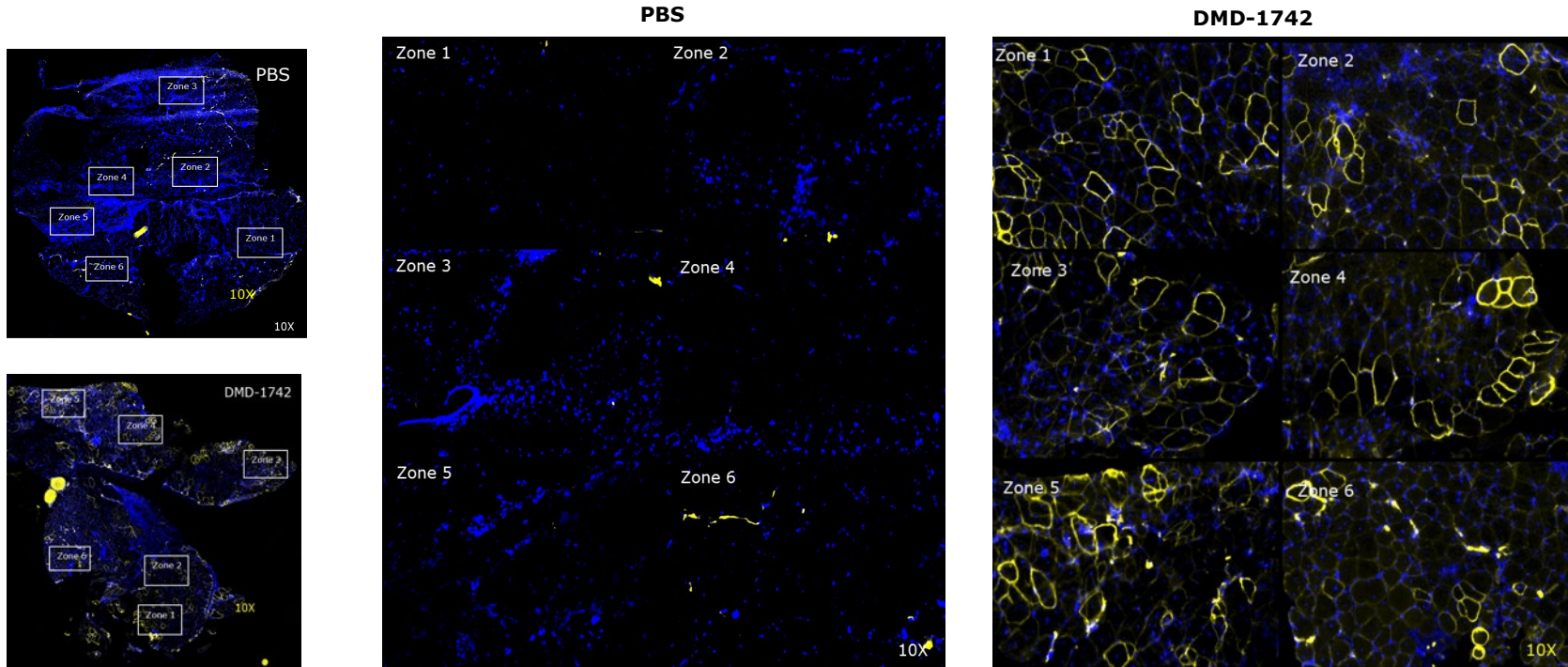
***In vivo* dystrophin protein restoration (drisapersen surrogate, 200 mg/kg, 8 weekly IV doses)**



- Less than 1.5% dystrophin restoration in two separate studies^{1,2}
- No reduction in CK levels¹

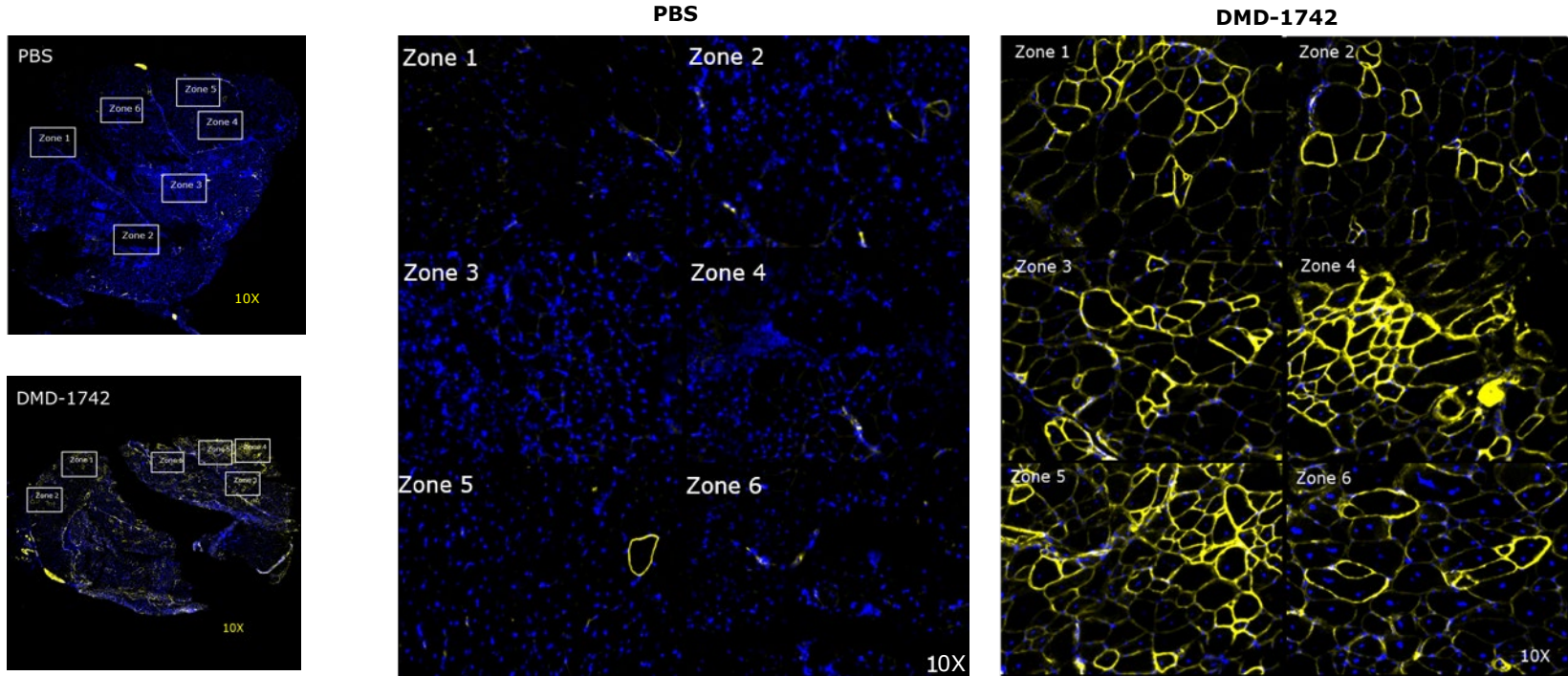
Single dose of surrogate results in restoration of dystrophin in muscle fibers

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



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

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



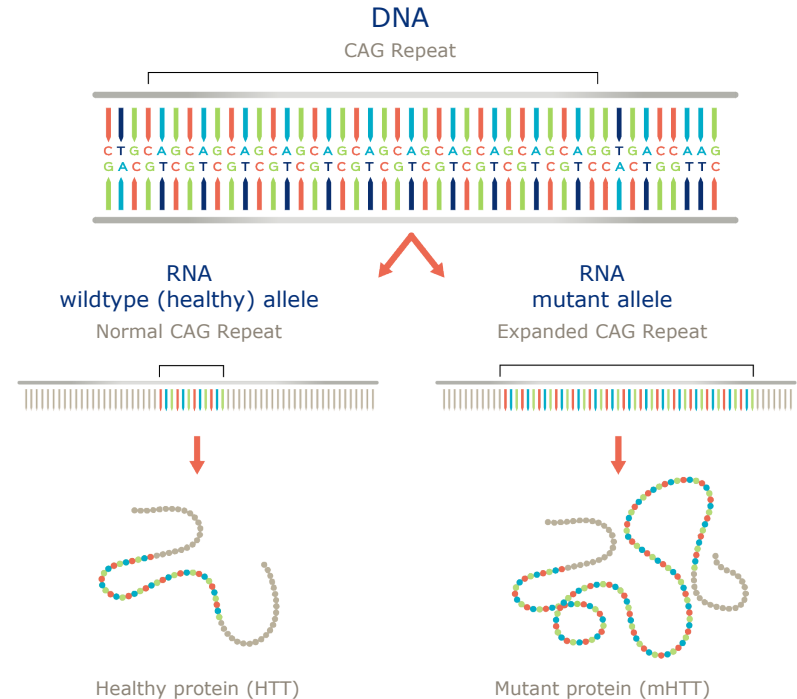
WVE-120101

WVE-120102

Huntington's Disease

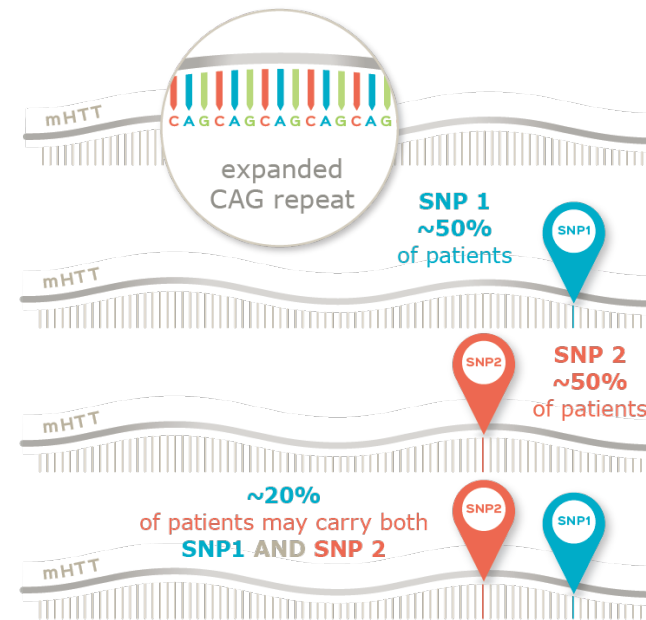
Huntington's disease: a hereditary, fatal disorder

- 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



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)



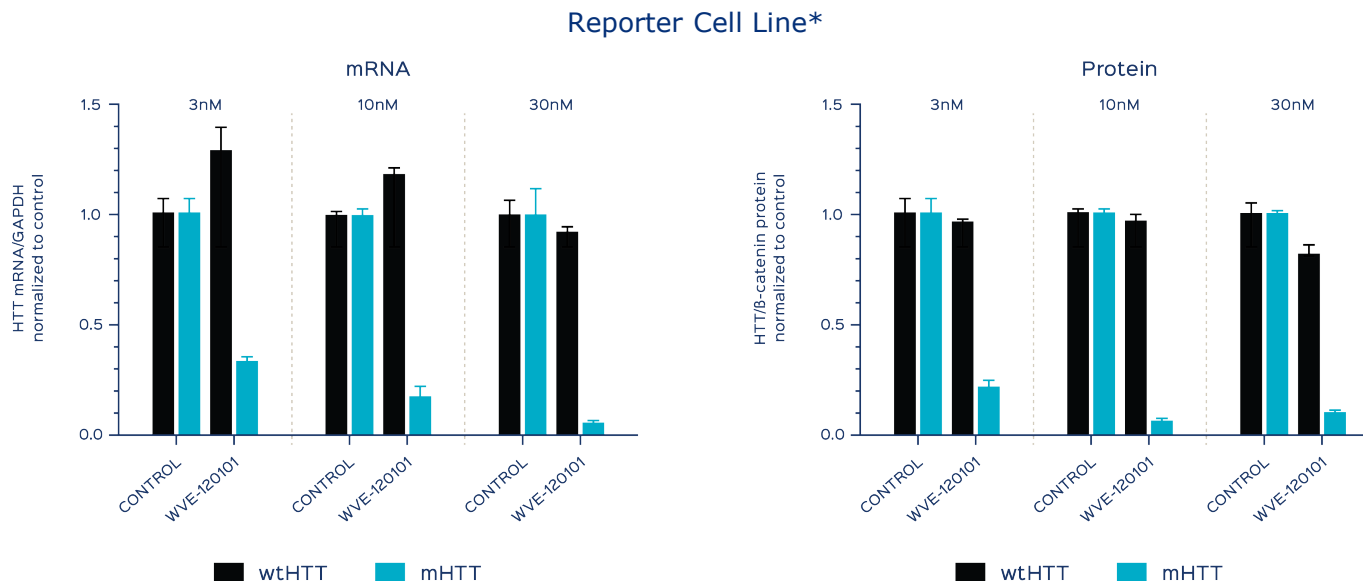
Total: Due to overlap, an estimated **~70%** of the total HD patient population carry SNP 1 and/or SNP 2

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 by YE 2019

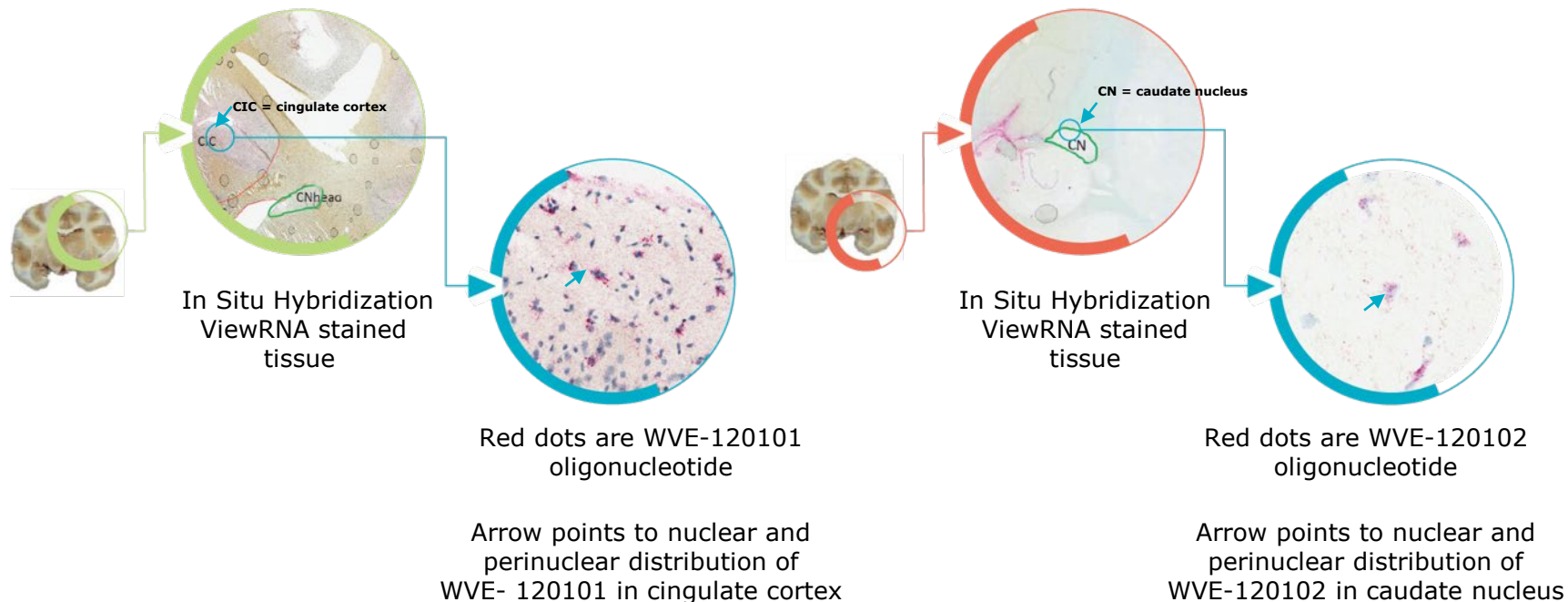
Selective reduction of mHTT mRNA & protein



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

Demonstrated delivery to brain tissue

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



WVE-C092

Amyotrophic Lateral Sclerosis (ALS)
Frontotemporal Dementia (FTD)

C9orf72: a critical genetic risk factor

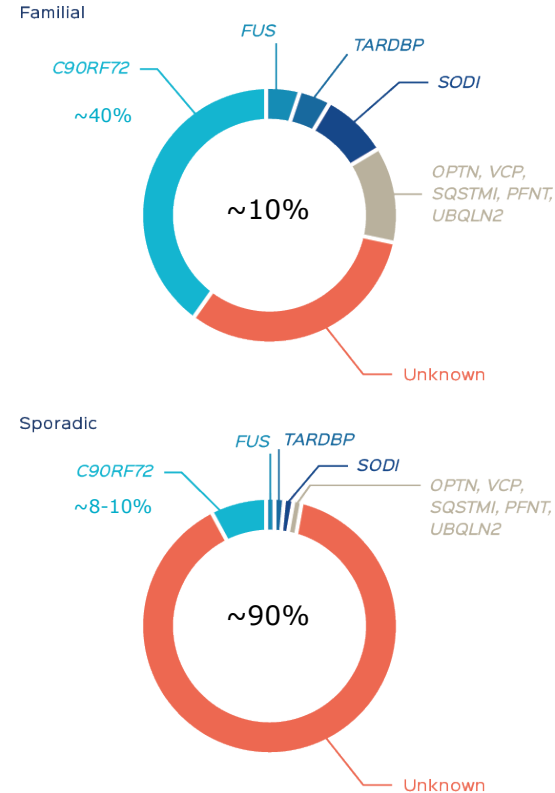
- C9orf72 gene provides instructions for making protein found in various tissues, with abundance in nerve cells in the cerebral cortex and motor neurons
- C9orf72 genetic mutations are the strongest genetic risk factor found to date for the more common, non-inherited (sporadic) forms of Amyotrophic Lateral 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



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

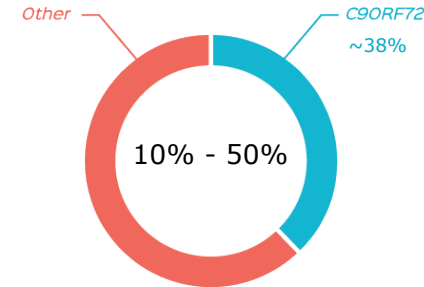
Clinical development expected to initiate in 2H 2020



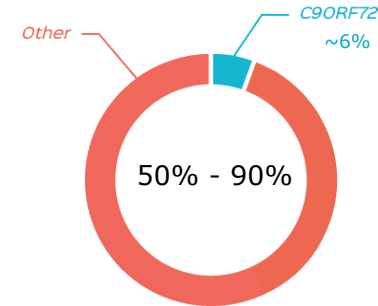
Frontotemporal dementia

- 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

Familial



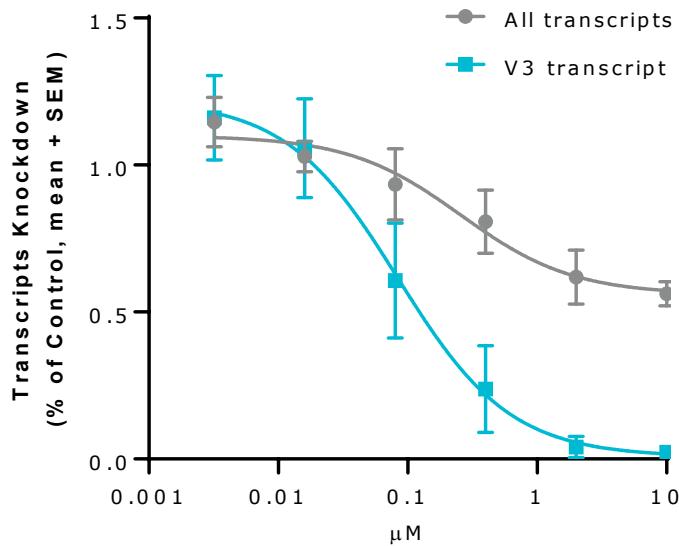
Sporadic



Clinical development expected to initiate in 2H 2020

WVE-C092 demonstrated selective and potent silencing of expanded C9orf72 repeat transcripts

WVE-C092 preferentially reduces repeat-containing V3 transcripts



Stereochemistry and chemistry optimization improves potency

IC ₅₀ (nM)	
WVE-C092	84
WVE-3972-01	411
Stereorandom ASO	845

10-fold

Ophthalmology

Building a portfolio for inherited retinal diseases

Inherited retinal diseases (IRDs)

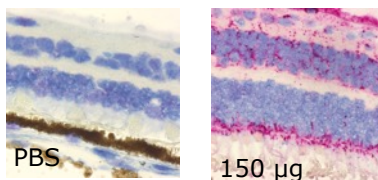
- Rare eye disorders caused by genetic mutations leading to progressive vision loss
- No approved therapies for almost any IRDs
- Approximately 200,000 affected in the U.S. and millions world-wide

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

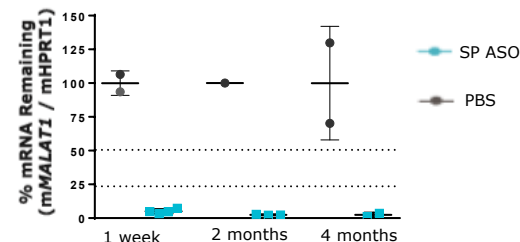
Single IVT injection of stereopure oligonucleotide to NHP results in distribution throughout all layers of the retina and potent, extended duration of effect

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 2H 2019

Anticipated upcoming Wave milestones

Neuromuscular

- **July 2019:** Initiation of DYSTANCE 51 Phase 2/3 clinical trial for suvodirsen in DMD (exon 51)
- **2H 2019:** Interim dystrophin data readout for suvodirsen from OLE in DMD (exon 51)
- **2H 2020:** Accelerated approval filing for suvodirsen in DMD (exon 51) in US, pending positive clinical dystrophin expression data
- **2H 2020:** Topline clinical data for WVE-N531 in DMD (exon 53)

CNS

- **By YE 2019:** Topline data readout from PRECISION-HD Phase 1b/2a trials in Huntington's disease
- **2H 2020:** Initiation of clinical development of WVE-C092 (C9orf72) in ALS and FTD

Ophthalmology

- **2H 2019:** Selection of initial development candidate for inherited retinal disease



Realizing the potential of genetic medicines

For more information:

Kate Rausch, Investor Relations
krausch@wavelifesci.com
617.949.4827

