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Parent Project Muscular Dystrophy Annual Conference June 29, 2018

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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Introduction to Wave

Biotechnology company developing targeted therapies for patients impacted by rare diseases

- Founded in 2009 – merger of Chiralgen and Ontorii
- Rationally designed stereopure nucleic acid therapeutics
- Utilizing multiple modalities including antisense, exon skipping and RNAi
- Expertise and core focus in neurology
- DMD Exon 51 Phase 1 trial ongoing, safety data expected Q3 2018
- DMD Exon 53 Phase 1 trial expected to initiate in Q1 2019
- Active research in additional DMD exon skipping approaches underway
- In-house manufacturing capability ranging from high throughput to large scale GMP production

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Our growing pipeline is focused primarily on neuromuscular and central nervous system disorders

	TARGET	BIOMARKER	MECHANISM	DISCOVERY	CANDIDATE	CLINICAL	TRIAL PHASE
CNS							
Huntington's disease	mHTT SNP1	mHTT	A	●	●	●	Phase 1b/2a
Huntington's disease	mHTT SNP2	mHTT	A	●	●	●	Phase 1b/2a
Amyotrophic lateral sclerosis	C9orf72	Dipeptide	A	●	●	○	
Frontotemporal dementia	C9orf72	Dipeptide	A	●	●	○	
Spinocerebellar ataxia 3	ATXN3		S	●	○	○	
CNS diseases	Multiple†		○	●	○	○	
MUSCLE							
Duchenne muscular dystrophy	Exon 51	Dystrophin	E	●	●	●	Phase 1
Duchenne muscular dystrophy	Exon 53	Dystrophin	E	●	○	○	
Neuromuscular diseases	Multiple		○	●	○	○	
OPHTHALMOLOGY							
Retinal diseases	Multiple		○	●	○	○	
HEPATIC							
Metabolic liver diseases	APOC3	Triglyceride	S	●	○	○	
Metabolic liver diseases	Multiple (4)‡		○	●	○	○	

(S) = silencing. (A) = allele-specific silencing. (E) = exon skipping.

† 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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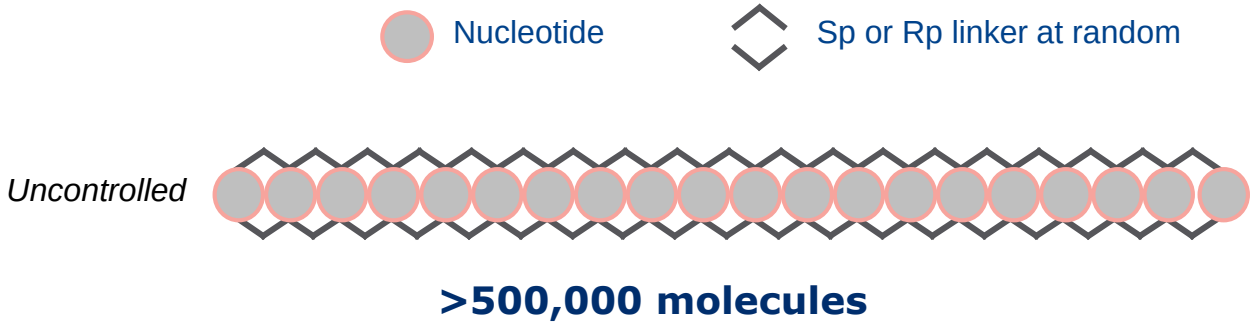
Building oligonucleotides

- Each oligonucleotide is made of strings of nucleotides (typically 20) held together by **chemical linkages**
- Linkages can be modified by phosphorothioate or morpholino chemistry
- With traditional synthesis methods, the **orientation of atoms at each linkage occurs randomly**, adopting either an "left" (Sp) or "right" (Rp) orientation
- This results in a mixture of >500,000 molecules (2^{19})
- Random orientations have implications for drug stability, efficacy, and safety



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Building optimized and stereopure oligonucleotides

STANDARD OLIGONUCLEOTIDE APPROACHES (PS, PMO, etc.)

Pharmacologic properties include >500,000 permutations in every dose

↓

Impact:
Unreliable therapeutic effects
Unintended off-target effects

WAVE RATIONAL DESIGN

Stereochemistry enables precise control, ability to optimize critical constructs into one defined and consistent profile

↓

Impact:
Potential for safer, more effective, targeted medicines that can address difficult-to-treat diseases

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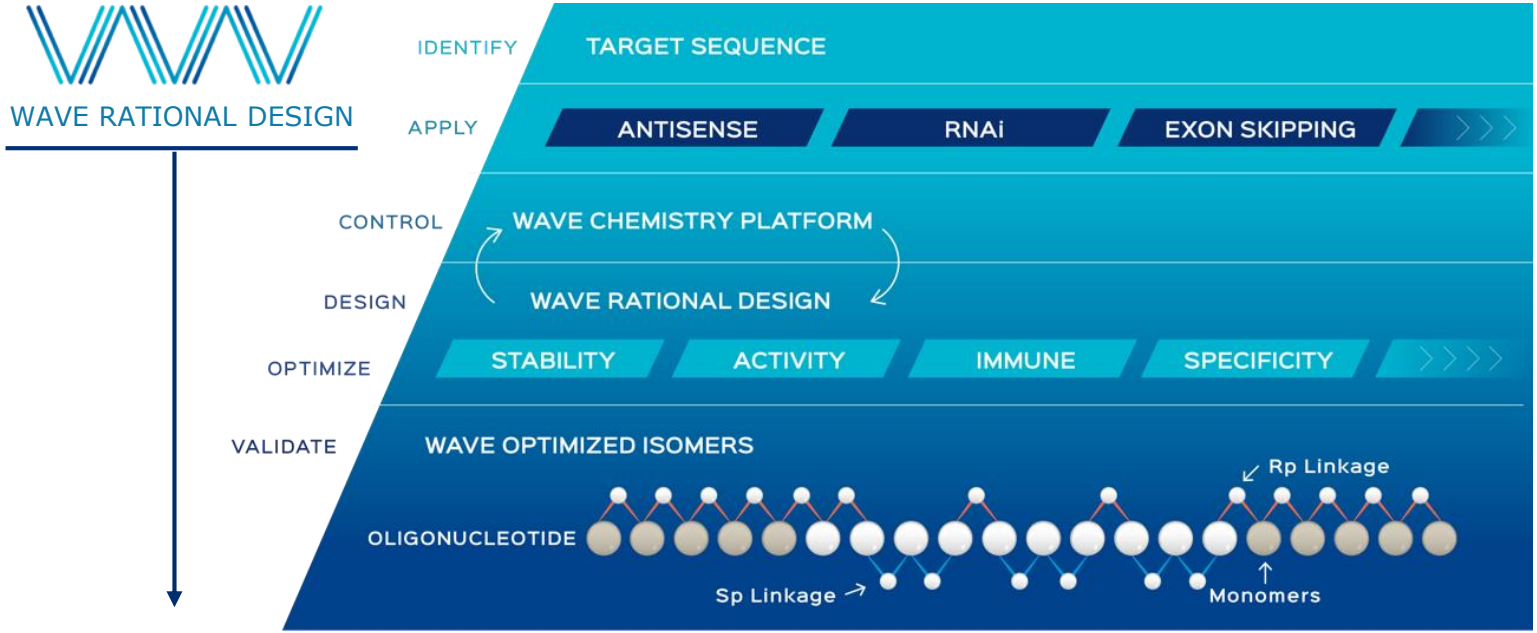
Creating a new class of potential therapies

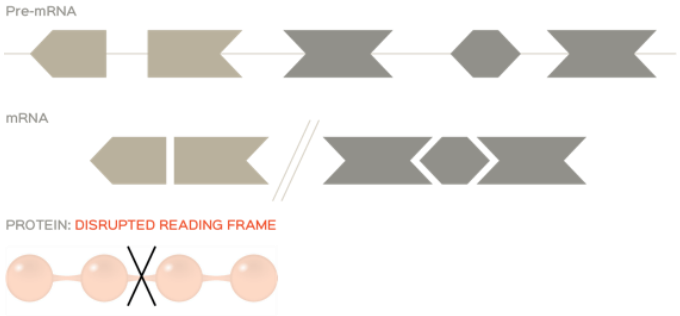


Source: Iwamoto N, et al. Control of phosphorothioate stereochemistry substantially increases the efficacy of antisense oligonucleotides. *Nature Biotechnology*. 2017;35:845-851.

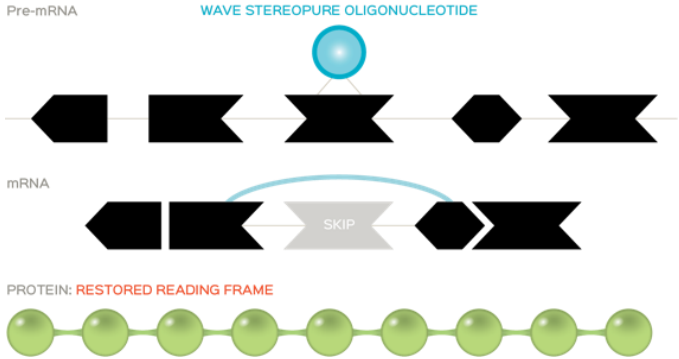
Exon skipping therapeutic approach

- Exon skipping approaches have the goal of enabling natural production of functional dystrophin protein
- Partial restoration of dystrophin is expected to result in therapeutic benefit

Dysfunctional splicing



Exon skipping approach



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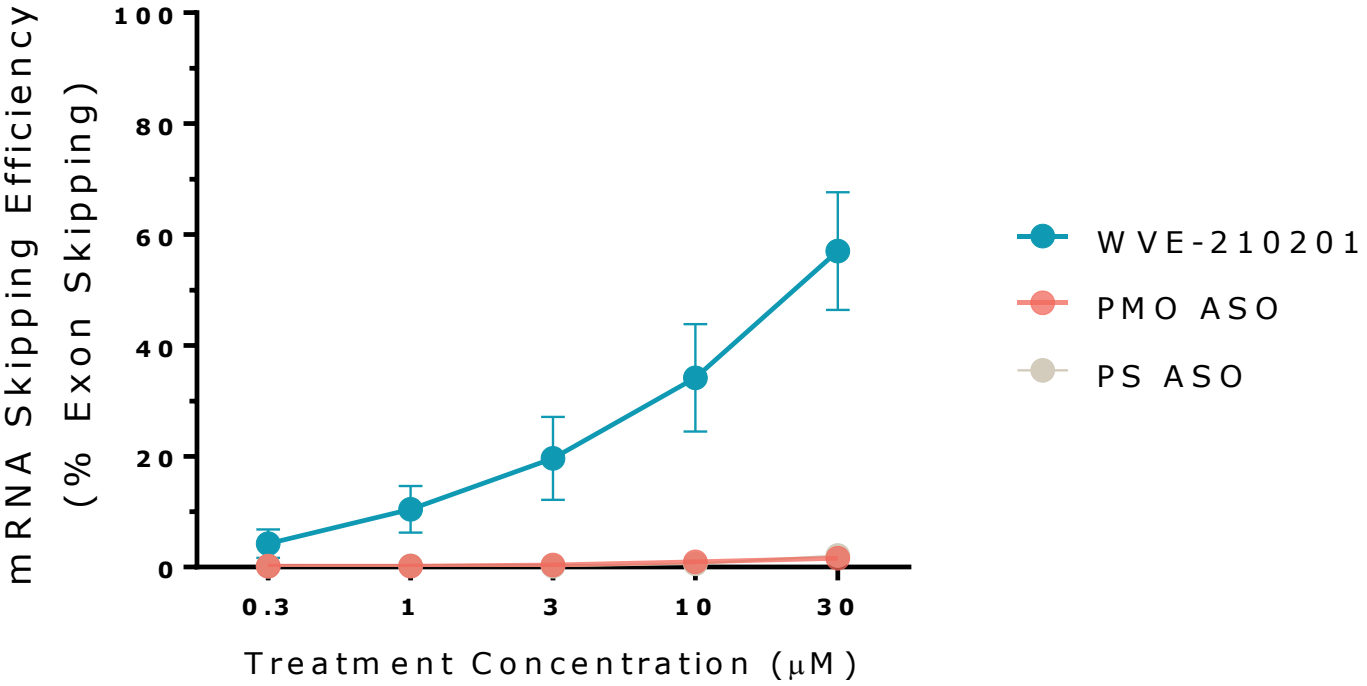
WVE-210201
An investigational stereopure exon 51 targeted oligonucleotide

WVE-210201 induces dose-dependent exon skipping *in vitro*



Data derived from *in vitro* preclinical research; WVE-210201 currently being evaluated in clinical studies.
Methods: Free uptake of ASO in human DMD myoblast cells. Skipping quantified by TaqMan assay.
PMO ASO = Morpholino Antisense Oligonucleotide; PS ASO = Phosphorothioate Antisense Oligonucleotide.

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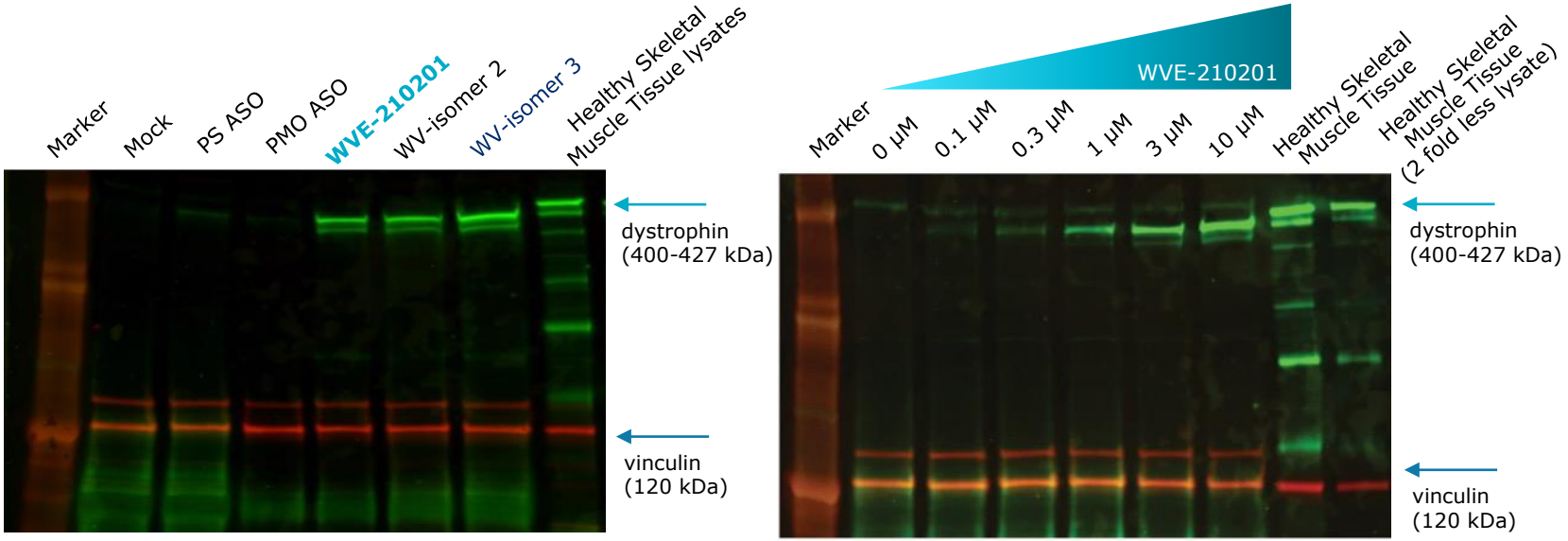
WVE-210201 increases natural dystrophin production *in vitro*

Green bands below show level of natural dystrophin protein expression with brighter/bolder bands indicating more protein expression



Data derived from *in vitro* preclinical research; WVE-210201 currently being evaluated in clinical studies.
Methods: Free uptake of ASO in human DMD myoblasts (Δ48-50). Protein expression determined by western blot.
PMO ASO = Morpholino Antisense Oligonucleotide; PS ASO = Phosphorothioate Antisense Oligonucleotide.

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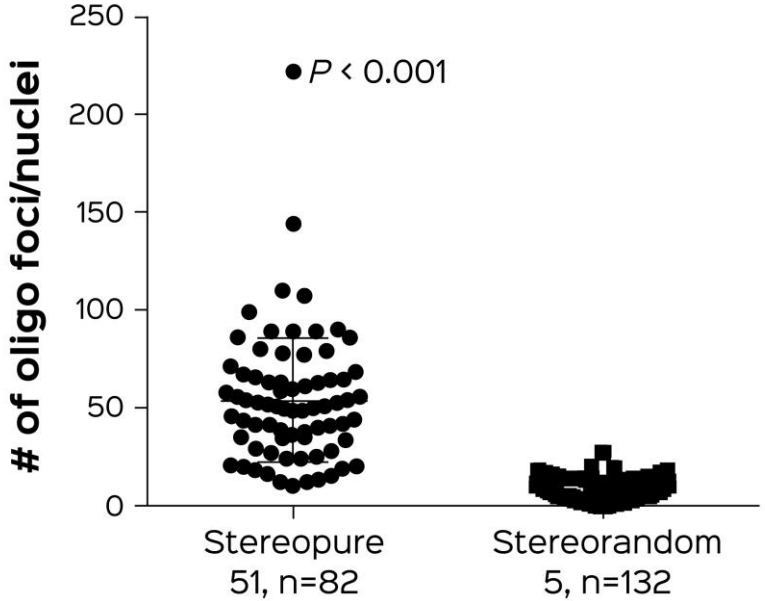
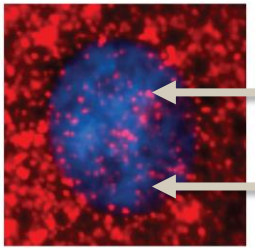
Wave's chemistry improves oligonucleotide uptake in the nucleus where splicing occurs

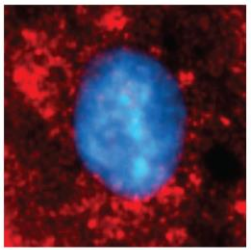
Stereopure oligonucleotides are designed to readily enter the nuclei of cells under free-uptake conditions, which approximates natural delivery in the body

Free uptake of stereorandom and stereopure ASOs





Stereopure



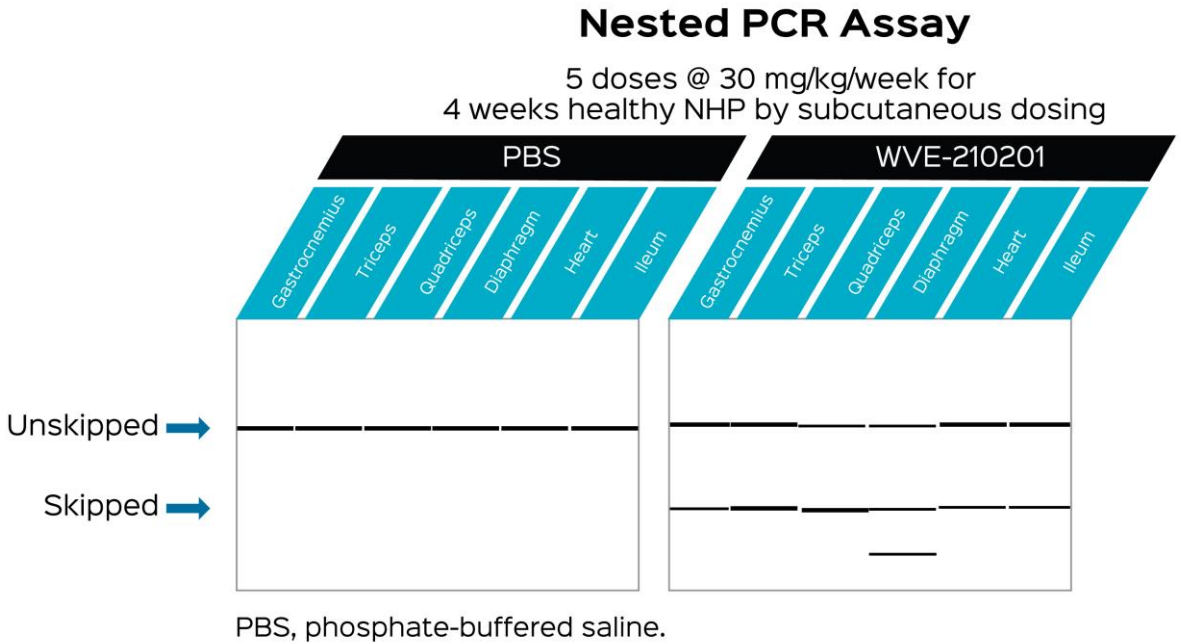
Stereorandom

Red
Oligonucleotide

Blue
Nucleus

Data derived from *in vitro* preclinical research; WVE-210201 currently being evaluated in clinical studies.
Methods: Free uptake of ASOs in 18 hour differentiating human DMD myoblasts (Δ48-50).

WVE-210201 produces exon skipping in multiple muscle tissues including heart muscle in monkeys



Data derived from *in vitro* preclinical research; WVE-210201 currently being evaluated in clinical studies.

Methods: Healthy monkeys received 5 doses of 30 mg/kg/week SC for 4 weeks. Muscle tissues were collected 2 days after the last dose.

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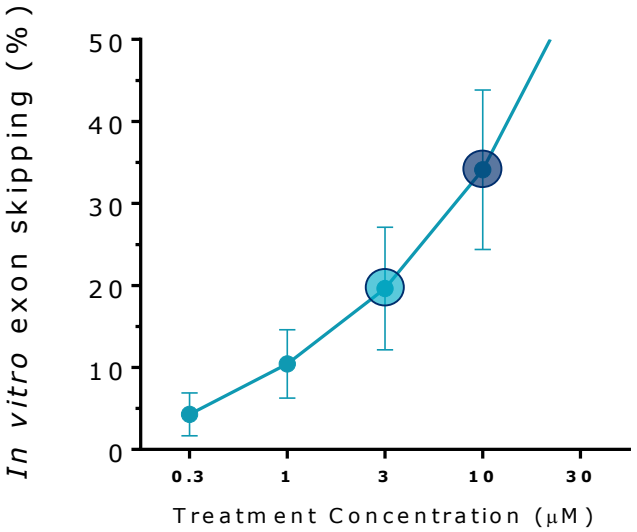
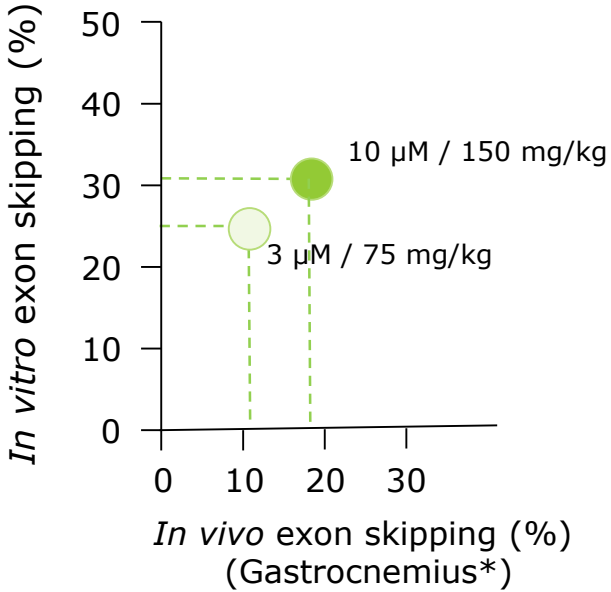
WVE-210201 supported by correlation of *in vitro* and *in vivo* data in *mdx 23* mice

WVE-210201
In vitro exon 51 skipping



In vivo exon skipping data not available

Surrogate Stereopure Oligonucleotide (WV-1)
In vitro and *in vivo* exon 23 skipping



*Representative muscle tissue
Methods: *In vitro* - Free uptake of ASO in human DMD myoblast cells. *In vivo* - 4 weekly IV dosing. Necropsy 96h post last dose. RNA skipping efficiency determined by Taqman assay.

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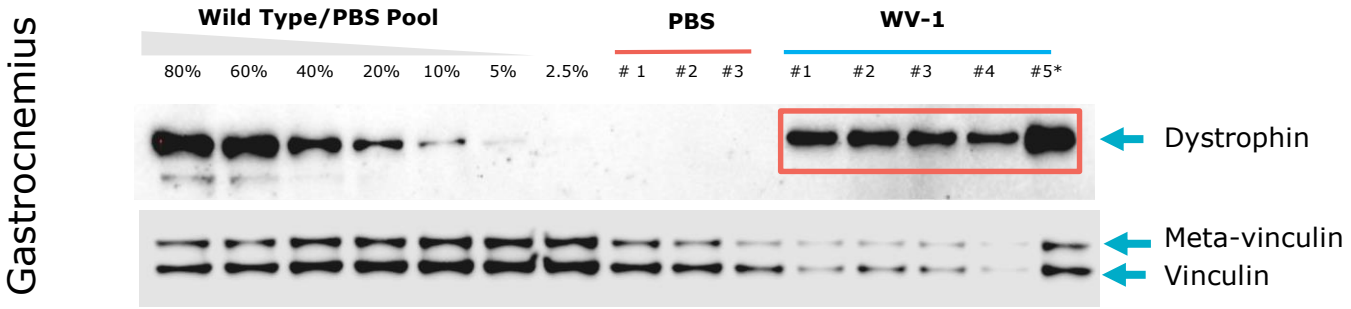
Exon skipping efficiency yields substantial natural dystrophin protein restoration in *mdx 23* mice

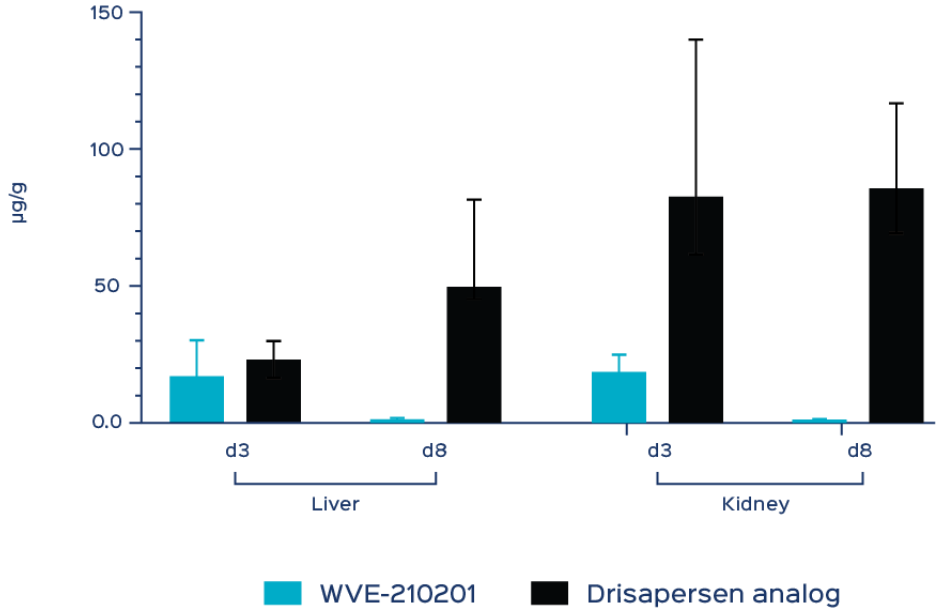
Surrogate stereopure oligonucleotide restored 70-90% of natural dystrophin production *in vivo*



*Numbers indicate individual animals
Methods: *mdx* 23 mice received 4 weekly IV doses (150 mg/kg). Tissues collected 96 hours post final dose. Protein expression determined by western blot.

WVE-210201 clears rapidly from liver and kidney in mice

Single *in vivo* IV dose at 30 mg/kg in *mdx* 23 mice



- WVE-210201 shows faster clearance from liver and kidney compared with a drisapersen analog made by Wave
- Wave's stereopure oligonucleotides can be optimized to allow faster clearance

Data derived from *in vivo* preclinical research; WVE-210201 currently being evaluated in clinical studies.
Methods: *mdx 23* mice received a single dose of ASO 30 mg/kg IV.

WVE-210201 Phase 1 clinical trial

ClinicalTrials.gov Identifier: NCT03508947

Design		
Methods	Global, randomized, double-blind, placebo-controlled, single ascending dose Phase 1 study	
Endpoints	**Primary**	Safety and tolerability
	Secondary	Pharmacokinetics
Study Sites	North America, Europe	
Dosing	3:1 randomization to WVE-210201 or placebo by IV infusion	

Key Enrollment Criteria

- Boys ages 5 to 18, amenable to exon 51 skipping
- Ambulatory and non-ambulatory
- Prior treatment with eteplirsen and ataluren allowed (following appropriate washout period)
- Prior treatment with drisapersen excluded
- Must be on a stable steroid regimen ≥1 month prior to enrollment

- **Safety data expected in Q3 2018**
- **Participants eligible for planned open-label extension study with muscle biopsy**

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WVE-210201 Next Steps

- Next WVE-210201 study is being designed with the DMD community and regulators
  - Design: Double-blind, placebo-controlled, multi-dose study assessing dystrophin expression and clinical outcomes
  - Measurement of dystrophin via standardized Western Blot
  - Interim analysis of dystrophin expression in muscle biopsies
  - Efficacy data readout anticipated H2 2019

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Wave's Progress in DMD

Stereopure oligonucleotides for DMD

- Wave's chemistry platform allows us to precisely design, optimize and manufacture stereopure oligonucleotides
- Stereopure molecules are intended to enhance the efficiency of exon skipping, with the goal of delivering and maintaining meaningful levels of natural dystrophin protein restoration
- Learnings from WVE-210201 and surrogate stereopure oligonucleotides are being applied to Wave's exon 53 and future DMD programs

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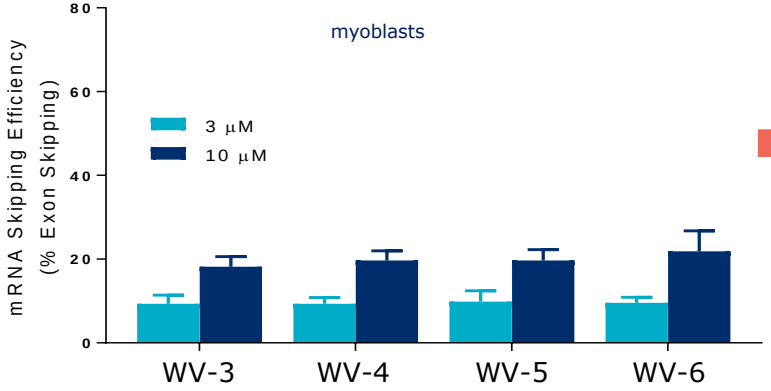
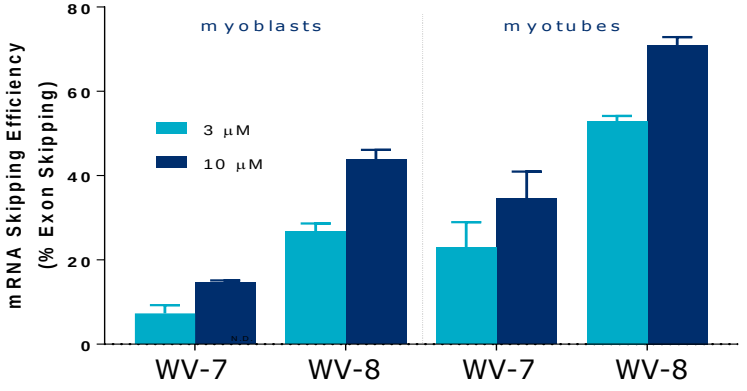
Exon 53: Stereopure lead molecules demonstrate increasing exon skipping efficiency

Initial Potential Candidates



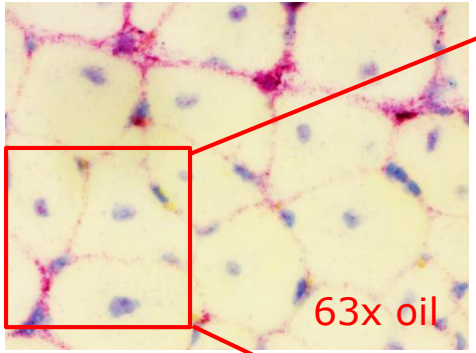
Most Recent Potential Candidates



Data derived from *in vitro* preclinical research.

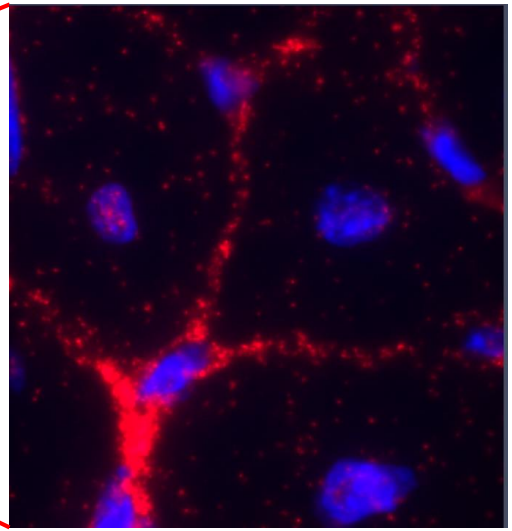
Methods: Free uptake of ASOs in a DMD patient-derived Δ45-52 cell line. Skipping determined by TaqMan assay.

Exon 53 targeting oligonucleotides rapidly distribute to muscle (24 hours after IV injection)



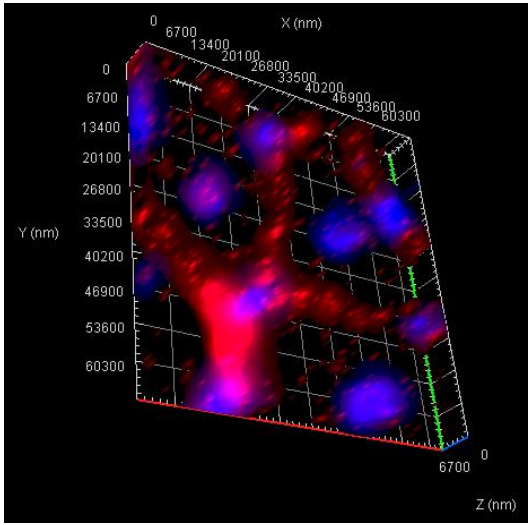
Bright field view

Nucleus: Hematoxylin; Light Blue
WV-7: ViewRNA, Fast Red



Fluorescence channel view

Nucleus: Hoechst33342; Blue
WV-7: Fast Red/Cy3; Pink Red



Z Stack view

Data derived from *in vivo* preclinical research.

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

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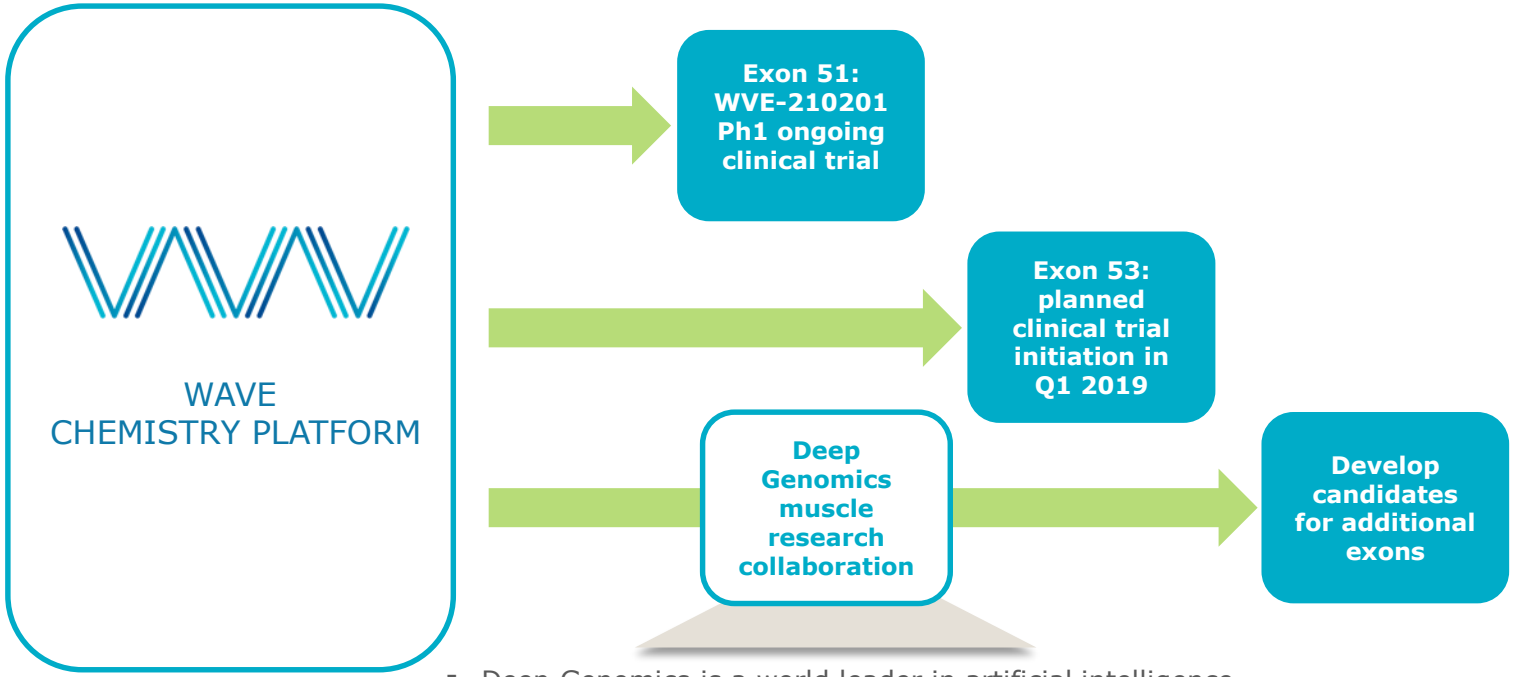
Wave's commitment to DMD



- Deep Genomics is a world leader in artificial intelligence
- Collaboration to identify new muscle targets, and optimal regions or sequences within those targets, to be addressed by Wave's stereopure oligonucleotides
- The goal is to help as many patients as possible

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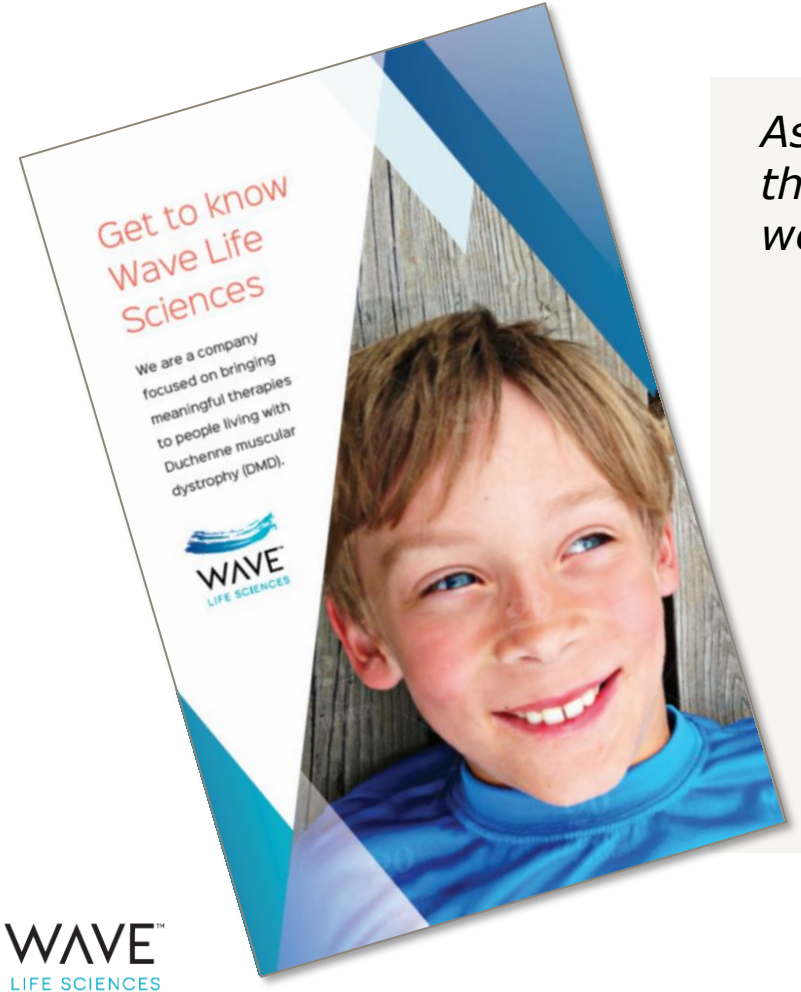

As we work to advance potential therapies for boys with DMD we will continue to:

- **Put patients' and families' best interests first**
- **Be good listeners and trusted community partners**
- **Move with a true sense of urgency**

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