Forward looking statements

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

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<th>MECHANISM</th>
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<th>TRIAL PHASE</th>
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**MUSCLE**

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**OPHTHALMOLOGY**

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**HEPATIC**

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- **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.
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
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
Creating a new class of potential therapies

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**
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.
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.


PMO ASO = Morpholino Antisense Oligonucleotide; PS ASO = Phosphorothioate Antisense Oligonucleotide.
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.

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

*Representative muscle tissue

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

- 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

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

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

<table>
<thead>
<tr>
<th>Design</th>
<th>Key Enrollment Criteria</th>
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<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Global, randomized, double-blind, placebo-controlled, single ascending dose Phase 1 study</td>
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<td><strong>Endpoints</strong></td>
<td><strong>Primary</strong> Safety and tolerability</td>
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<td><strong>Secondary</strong> Pharmacokinetics</td>
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<td><strong>Study Sites</strong></td>
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<tr>
<td><strong>Dosing</strong></td>
<td>3:1 randomization to WVE-210201 or placebo by IV infusion</td>
</tr>
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</table>

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

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.
Wave’s commitment to DMD

- Exon 51: WVE-210201 Ph1 ongoing clinical trial
- Exon 53: planned clinical trial initiation in Q1 2019

Deep Genomics muscle research collaboration

- Develop candidates for additional exons

- 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
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