Wave Life Sciences

Muscular Dystrophy Association
Clinical and Scientific Conference
Investor Update

April 16, 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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Paul Bolno, MD, MBA
President and CEO

Wave Life Sciences: Seeking to transform DMD treatment with stereopure exon skipping approach

Exon 51: Wave's lead development program in DMD

- High unmet need remains for ~13% of boys with DMD amenable to exon 51 skipping
- Developing stereopure exon therapies to be more potent than available treatments, without comprising safety
- Preclinical *in vitro* and *in vivo* models support ability to restore meaningful production of functional dystrophin protein
- Established US and EU regulatory paths

Building a fully integrated genetic medicines company

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Safety and Tolerability of Suvodirsen (WVE-210201) in Patients With Duchenne Muscular Dystrophy: Results From a Phase 1 Clinical Trial

Michael Panzara, MD, MPH
Chief Medical Officer

Study Objective

Primary Objective

- To evaluate the safety and tolerability of single ascending doses of suvodirsen in patients with Duchenne muscular dystrophy (DMD)

Secondary Objective

- To assess the pharmacokinetic (PK) profile of suvodirsen after single-dose administration

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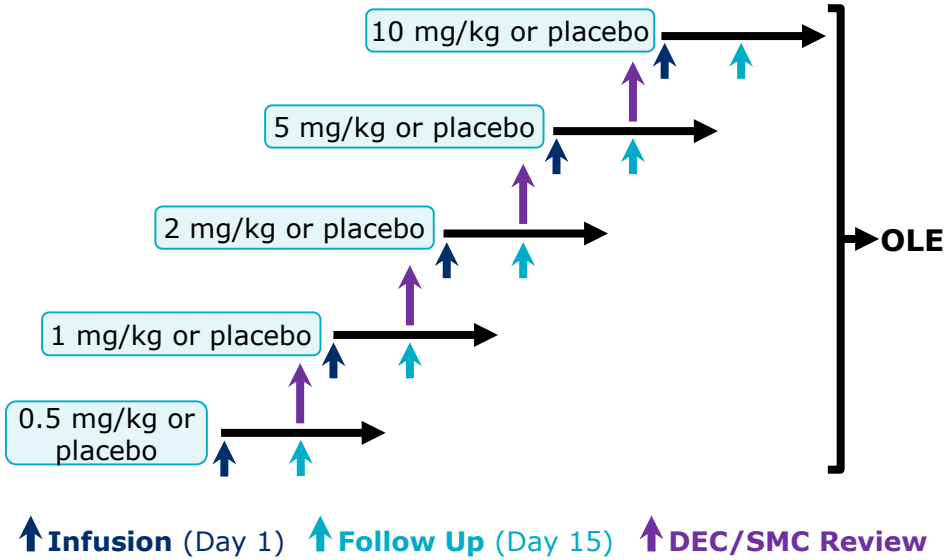
Study Design

- Phase 1, multicenter, double-blind, randomized, placebo-controlled trial with 12-week follow-up (NCT03508947) and optional open-label extension



- Staggered dosing, beginning with 2 sentinel patients observed for 48 h
- If neither experienced an SAE, remaining patients in the cohort were treated and observed for 24 h
- Dose escalation decision made based on the recommendation of the DEC and SMC
- Stopping criteria were based upon the European Guidelines for First-in-Human studies[1]
  - Single patient experienced an SAE assessed as related to treatment
  - ≥2 patients experienced treatment-emergent adverse event (AE) graded as severe and related to treatment

1. European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP). Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/07 Rev. 1.

AE=adverse event; DEC=Dose Escalation Committee; OLE=open-label extension; SAE=serious AE; SMC=Safety Monitoring Committee.

Key Enrollment Criteria

Key Inclusion Criteria

- Ambulatory and nonambulatory male patients
- 5–18 years old (inclusive)
- Confirmed *DMD* gene mutation amenable to exon 51 skipping
- May have been previously treated with eteplirsen or ataluren, with appropriate washout

Key Exclusion Criteria

- Prior treatment with drisapersen or gene therapy

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Study Endpoints

Primary Endpoint

- Safety and tolerability of suvodirsen, compared with placebo, as assessed by
  - Number (%) of patients with AEs
  - Severity of AEs
  - Number (%) of patients with SAEs
  - Number (%) of patients who withdrew due to AEs

Secondary Endpoint

- Assessment of PK parameters following single dose administration of suvodirsen

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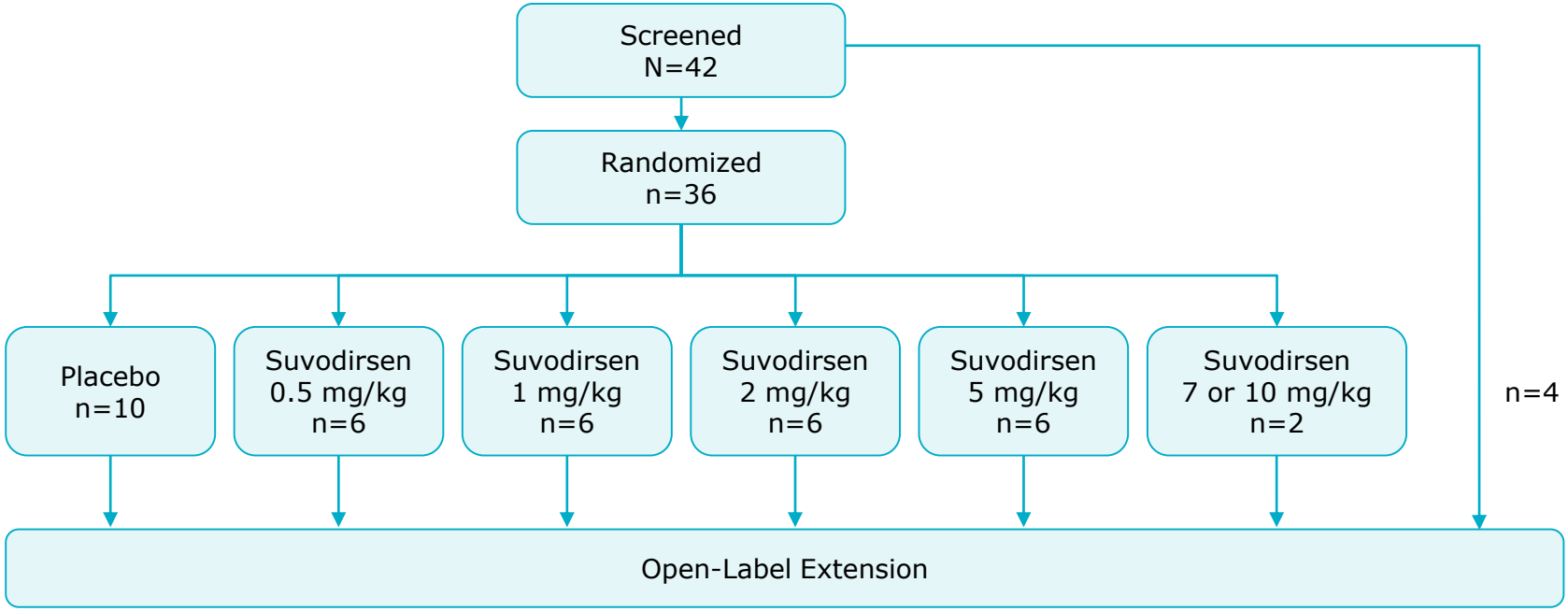
AE=adverse event; PK=pharmacokinetic; SAE=serious AE.

Patient Disposition



Baseline Demographic and Clinical Characteristics

Characteristic	Placebo n=10	Total Suvodirsen n=26
Age, mean (SD), y	8.5 (1.72)	8.0 (2.24)
Time since diagnosis, mean (SD), y	4.8 (3.25)	4.6 (2.64)
Ambulatory, n (%)	9 (90.0)	22 (84.6)
Prior treatment, n (%)	10 (100.0)	26 (100.0)
Eteplirsen	1 (10.0)	5 (19.2)
Deflazacort	8 (80.0)	22 (84.6)
Oral prednisone	2 (20.0)	6 (23.1)

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Incidence of Patients With Adverse Events

Event, n (%)	Placebo n=10	Suvodirsen 0.5 mg/kg n=6	Suvodirsen 1 mg/kg n=6	Suvodirsen 2 mg/kg n=6	Suvodirsen 5 mg/kg n=6
Patients with any AE	8 (80.0)	3 (50.0)	5 (83.3)	4 (66.7)	4 (66.7)
Mild	6 (60.0)	3 (50.0)	5 (83.3)	4 (66.7)	2 (33.3)
Moderate	0.0	0.0	0.0	0.0	2 (33.3)
Severe	2 (20.0)	0.0	0.0	0.0	0.0
Serious AE	1 (10.0)	0.0	0.0	0.0	0.0
Discontinued due to TEAE	0.0	0.0	0.0	0.0	0.0
Death	0.0	0.0	0.0	0.0	0.0

- Suvodirsen was generally safe and well tolerated up to and including 5 mg/kg
- No serious AEs, discontinuations due to AEs, or deaths in suvodirsen-treated patients

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Adverse Events Occurring in ≥2 Patients in an Active Treatment Group

AE, n (%)	Placebo n=10	Suvodirsen 0.5 mg/kg n=6	Suvodirsen 1 mg/kg n=6	Suvodirsen 2 mg/kg n=6	Suvodirsen 5 mg/kg n=6
Any AE	8 (80.0)	3 (50.0)	5 (83.3)	4 (66.7)	4 (66.7)
Any AE occurring in ≥2 patients in an active treatment group					
Pyrexia	0.0	0.0	0.0	0.0	4 (66.7)
Headache	0.0	0.0	2 (33.3)	1 (16.7)	3 (50.0)
Vomiting	0.0	1 (16.7)	0.0	0.0	2 (33.3)
Tachycardia	1 (10.0)	0.0	0.0	0.0	1 (16.7)

- The most common AEs were headache, pyrexia, vomiting, and tachycardia
  - The majority were infusion-associated reactions (IARs), defined as events occurring within 24 h of start of infusion

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Infusion-Associated Reactions

IAR, n (%)	Placebo n=10	Suvodirsen 0.5 mg/kg n=6	Suvodirsen 1 mg/kg n=6	Suvodirsen 2 mg/kg n=6	Suvodirsen 5 mg/kg n=6
Any IAR	2 (20.0)	0.0	3 (50.0)	1 (16.7)	4 (66.7)
IAR occurring in ≥2 patients in any treatment group					
Pyrexia	0.0	0.0	0.0	0.0	4 (66.7)
Headache	0.0	0.0	1 (16.7)	0.0	3 (50.0)
Vomiting	0.0	0.0	0.0	0.0	2 (33.3)
Tachycardia	1 (10.0)	0.0	0.0	0.0	1 (16.7)

- IARs included any AE with onset occurring within 24 h of start of infusion

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Dose Exploration Above 5 mg/kg Suvodirsen

- SMC endorsed exploration of a higher dose as planned per protocol
- A patient received 10 mg/kg infused over 1 hour
  - Patient experienced pyrexia (39.6°C), headache, tachycardia, and vomiting 4 h after EOI
  - Characterized by investigator as nonserious but severe
  - Patient was treated with 2 doses of hydrocortisone and acetaminophen with resolution of symptoms
- A patient then received 7 mg/kg infused over 2 hours, in the setting of pretreatment with hydrocortisone and acetaminophen
  - Patient experienced isolated pyrexia (39.5°C) with no other associated symptoms 6 hours after EOI
  - Characterized by investigator as nonserious but severe
  - Resolved with acetaminophen treatment
- IARs were associated with transient increases in hsCRP and complement factor Bb, with no change in complement C3
- Predefined stopping criteria met; SMC reviewed and agreed dosing could proceed at 5 mg/kg

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EOI=end of infusion; hsCRP=high-sensitivity C-reactive protein; IAR=infusion-associated reaction; SMC=Safety Monitoring Committee.

Conclusions

- Suvodirsen was generally safe and well tolerated at doses up to and including 5 mg/kg
  - Most common AEs were infusion-associated
    - Mild to moderate in intensity
    - Associated with transient increases in hsCRP and complement factor Bb
    - Resolved with symptomatic treatment
    - Increased severity at doses above 5 mg/kg
- Results from this first-in-human trial support the initiation of the global Phase 2/3 efficacy and safety trial of suvodirsen in patients with DMD amenable to exon 51 skipping (DYSTANCE 51)

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AE=adverse event; DMD=Duchenne muscular dystrophy; hsCRP=high-sensitivity C-reactive protein; IAR=infusion-associated reaction

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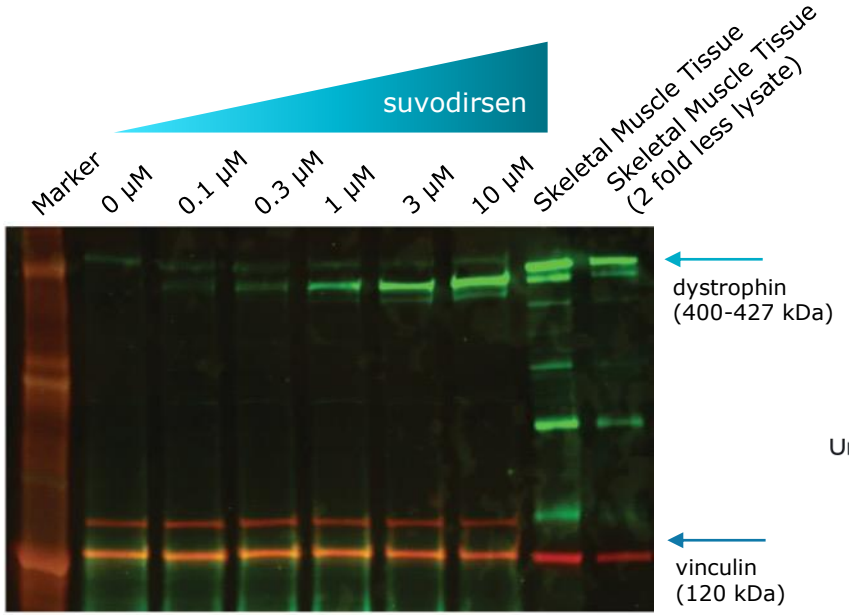
DYSTANCE 51: A Phase 2/3 Clinical Trial of Suvodirsen in Patients with Duchenne Muscular Dystrophy

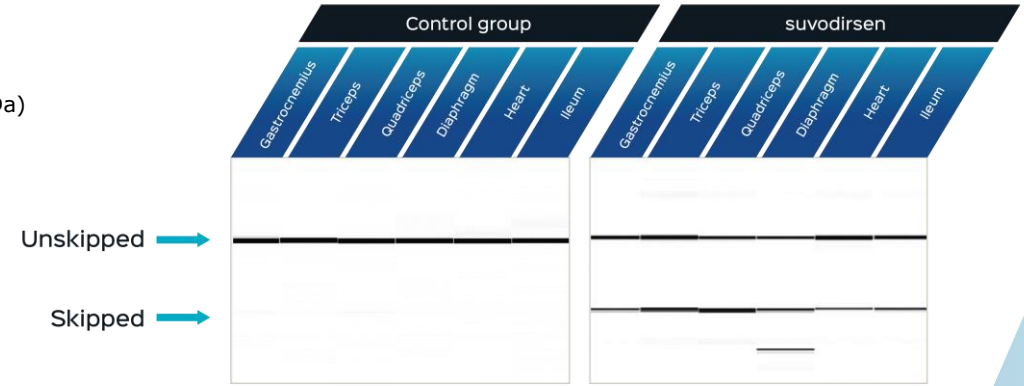
Suvodirsen Induces Potent Exon Skipping *in vitro* and *in vivo* Target Engagement in Healthy Nonhuman Primate



Experimental conditions: DMD protein restoration by Western Blot in patient-derived myotubes with clear dose effect.

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.

Preclinical and Clinical Data Used to Support Final Dose Selection in OLE and DYSTANCE 51

- *In vitro* studies of suvodirsen
- *In vivo* study of suvodirsen target engagement in normal monkey
- Multiple *in vitro* and *in vivo studies* in mdx23 mouse
- Human PK data from Phase 1 study of suvodirsen
  - Both tolerability data and PK profile

- **Conclusions:** Preclinical and clinical data support determination that doses of 3 mg/kg and 4.5* mg/kg are likely to provide meaningful levels of skipping and potential dystrophin restoration with differences between their tolerability profiles

Note: 4.5 mg/kg dose in DYSTANCE 51 provides approximately the same amount of active ingredient as the 5 mg/kg dose in the Phase 1 clinical trial

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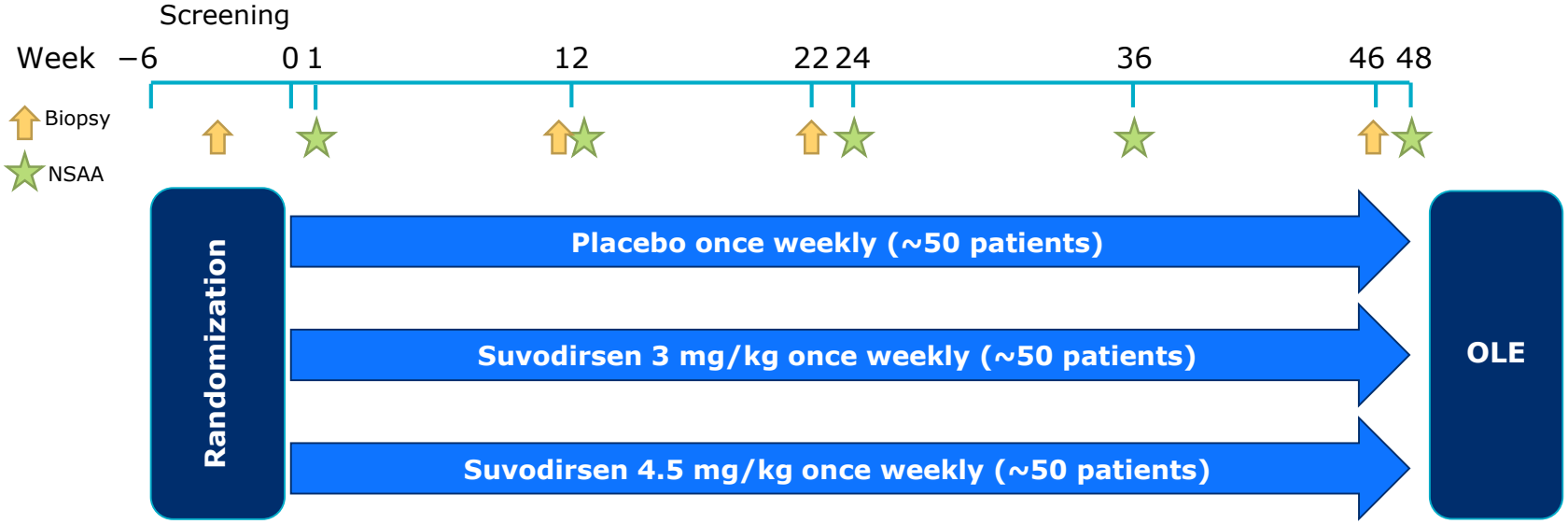
DYSTANCE 51 Phase 2/3 Trial Study Design



- The DYSTANCE 51 clinical trial has been selected for the US Food and Drug Administration Complex Innovative Trial Design Pilot Program

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DYSTANCE 51 Key Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Diagnosis of DMD with documented mutation amenable to exon 51 skipping
- Ambulatory male aged 5–12 years (inclusive)
- Able to walk independently for ≥10 meters in ≤20 seconds
- Stable pulmonary and cardiac function
- Stable systemic corticosteroid therapy regimen for ≥6 months with no changes in prior 3 months

Key Exclusion Criteria

- Severe cardiomyopathy
- Need or anticipated need for daytime mechanical or noninvasive ventilation
- Prior treatment with drisapersen, an investigational peptide-conjugated phosphorodiamidate morpholino oligomer, or gene therapy
- Treatment with ataluren or eteplirsen within 14 weeks before baseline biopsy
- Treatment with any investigational drug within 3 months or 5 half-lives, whichever is longer

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DMD=Duchenne muscular dystrophy

DYSTANCE 51 Study Endpoints

Primary

- US (and other regions, as applicable): Change from baseline in dystrophin protein levels (western blot of deltoid muscle) through 46 weeks
- EU (and other regions, as applicable): Change from baseline in NSAA through 48 weeks

Secondary

- Change from baseline through 48 weeks in
  - Key: NSAA (at 48 weeks) or dystrophin protein levels (at 46 weeks)
  - Upper limb proximal strength assessed by handheld myometry
  - Time to walk/run 10 meters
  - Time to preform 4-stair climb
  - Forced vital capacity (% predicted)
  - 95th percentile of stride velocity measured using the ActiMyo wearable device

Exploratory

- Change from baseline through 48 weeks in
  - PedsQL
  - Individual NSAA items
  - Respiratory function peak flow rate and cough peak flow
  - Upper limb function assessed by PUL 2.0
- Time to loss of ambulation, loss of self-feeding, and requirement for daytime ventilation on a regular basis
- Change from baseline in daily activity as measured by ActiMyo wearable device

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NSAA=North Star Ambulatory Assessment; PedsQL=Pediatric Quality of Life Inventory; PUL=Performance of the Upper Limb.

Conclusions

- Suvodirsen was generally safe and well tolerated at doses up to and including 5 mg/kg
  - Most common AEs were infusion-associated
    - Mild to moderate in intensity
    - Associated with transient changes in hsCRP and complement factor Bb
    - Resolved with symptomatic treatment
    - Increased severity at doses above 5 mg/kg
- Based on *in vitro* and *in vivo* preclinical studies and the Phase 1 clinical results, Wave selected 3 and 4.5 mg/kg for its planned Phase 2/3 clinical trial of suvodirsen
- Results from this first-in-human trial support the initiation of the global Phase 2/3 efficacy and safety trial of suvodirsen in patients with DMD amenable to exon 51 skipping (DYSTANCE 51)

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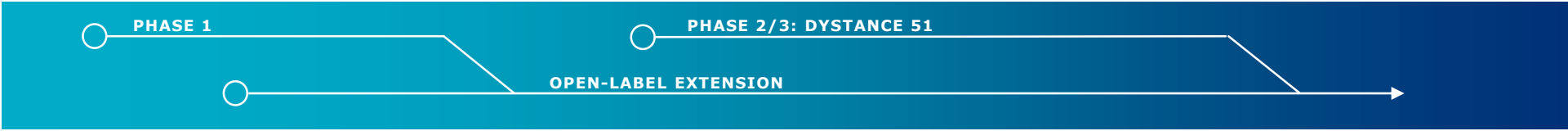
Note: 4.5 mg/kg dose in DYSTANCE 51 provides approximately the same amount of active ingredient as the 5 mg/kg dose in the Phase 1 clinical trial

Suvodirsen: Upcoming milestones



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 open to patients from Phase 1
- Data will be an important component of submission for accelerated approval in US
- **Interim analysis of dystrophin expression in 2H 2019**

DYSTANCE 51 (Phase 2/3)

- Phase 2/3 clinical trial to assess clinical efficacy and dystrophin expression
- Efficacy and safety data to serve as basis of regulatory submissions globally
- Selected for FDA pilot program for complex innovative trial designs
- **To be initiated in July 2019**

H2 2020: Potential FDA accelerated approval filing in exon 51 amenable DMD

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Suvodirsen formerly named WVE-210201

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