UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 16, 2019

WAVE LIFE SCIENCES LTD.
(Exact name of registrant as specified in its charter)

Singapore	**001-37627**	**Not Applicable**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
7 Straits View #12-00, Marina One East Tower Singapore 018936		**018936**
(Address of principal executive offices)		**(Zip Code)**

Registrant's telephone number, including area code: +65 6236 3388

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On April 16, 2019, Wave Life Sciences Ltd. (the "Company" or "Wave") issued a press release announcing the final results from its Phase 1 clinical trial of investigational suvodirsen (WVE-210201) in boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 51 skipping; details on the design of its planned Phase 2/3 clinical trial of suvodirsen in DMD, DYSTANCE 51; and providing an update on the Company's ongoing open-label extension study of suvodirsen. The press release also indicated that the Phase 1 data and DYSTANCE 51 clinical trial details will be presented on April 16, 2019 at the 2019 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in Orlando, FL.

In addition, the press release indicated that Wave management will host an investor conference call at 7:30 a.m. ET on April 16, 2019 to discuss the Phase 1 results and Phase 2/3 trial design. For purposes of the call, the Company provided an investor slide presentation (the "Investor Slide Presentation") summarizing the Phase 1 results and Phase 2/3 trial design, which is available on the "For Investors & Media" section of the Company's website at http://ir.wavelifesciences.com/. Copies of the press release and the Investor Slide Presentation are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and are incorporated by reference herein.

Item 8.01 Other Events.

The information set forth in the press release dated April 16, 2019, other than the second and sixth paragraphs thereof, is incorporated by reference into this Item 8.01 of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Document
99.1	Press Release issued by Wave Life Sciences Ltd. dated April 16, 2019
99.2	Investor Slide Presentation dated April 16, 2019

The portions of the press release incorporated by reference into Item 8.01 of this Current Report on Form 8-K are being filed pursuant to such item. The remaining portions of the press release are being furnished pursuant to Item 7.01 of this Current Report on Form 8-K and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that Section, nor shall they be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act except as shall be expressly set forth by specific reference in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

WAVE LIFE SCIENCES LTD.

By: */s/ Keith C. Regnante*
Keith C. Regnante
Chief Financial Officer

Date: April 16, 2019

Wave Life Sciences Announces Suvodirsen Phase 1 Safety and Tolerability Data and Phase 2/3 Clinical Trial Design

Data to be presented today at 2019 Muscular Dystrophy Association Clinical and Scientific Conference

Phase 2/3 clinical trial for suvodirsen in DMD expected to initiate in July 2019

Interim efficacy data from ongoing open-label extension study expected in H2 2019

Investor conference call scheduled for 7:30 a.m. ET today to discuss Phase 1 results and Phase 2/3 trial design

CAMBRIDGE, Mass., April 16, 2019 – Wave Life Sciences Ltd. (NASDAQ: WVE), a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases, today announced the final results from its Phase 1 clinical trial of investigational suvodirsen (WVE-210201) in boys with Duchenne muscular dystrophy (DMD) who are amenable to exon 51 skipping. The company also announced the design of its planned Phase 2/3 clinical trial of suvodirsen in DMD, DYSTANCE 51. The Phase 1 data and DYSTANCE 51 details will be presented today at the 2019 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in Orlando, Florida.

"We are delighted that suvodirsen's Phase 1 results demonstrate a favorable safety and tolerability profile that allow us to proceed rapidly into Phase 2/3 clinical development with doses we expect to be within the therapeutic window. Later this year, we expect to report interim efficacy data from the ongoing open-label extension study of suvodirsen and intend to use those data as an important component of a submission for accelerated approval in the United States," said Michael Panzara, MD, MPH, Chief Medical Officer of Wave Life Sciences. "We truly appreciate the boys and families that made this trial possible."

Phase 1 Clinical Trial Results

Wave's Phase 1 clinical trial was a global, multicenter, double-blind, placebo-controlled study designed to evaluate the safety, tolerability and plasma concentrations of single ascending doses of suvodirsen administered intravenously. Thirty-six patients received a dose of 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 5 mg/kg, 7 mg/kg or 10 mg/kg of suvodirsen (n=26) or placebo (n=10) in five ascending dose cohorts and were followed for 85 days. No serious adverse events, deaths or discontinuations due to adverse events were reported in any study patients treated with suvodirsen.

In December 2018, the company selected an initial dose for the DYSTANCE 51 Phase 2/3 clinical trial based on results from the first four cohorts (0.5 mg/kg – 5 mg/kg) of the Phase 1 clinical trial. Key findings from suvodirsen patients in those four cohorts (n=24) and all placebo patients (n=10) include:

- Suvodirsen was generally safe and well tolerated;
- 67% of patients who received suvodirsen (16/24) and 80% of patients who received placebo (8/10) experienced one or more adverse events;
- The most common adverse events occurring in two or more patients who received suvodirsen were pyrexia, headache, vomiting and tachycardia, consistent with infusion-associated reactions;
- Adverse events in patients receiving suvodirsen were mild to moderate in intensity and resolved spontaneously or with symptomatic treatment;

- No clinically relevant changes were observed in renal or hepatic parameters or platelet levels;
- In patients receiving 5 mg/kg of suvodirsen, the adverse events that occurred within 24 hours of infusion were associated with transient increases in high-sensitivity C-reactive protein and complement factor Bb levels, both of which were resolved within a week; and
- No changes were observed in complement C3 levels.

Based on results of the first four ascending dose cohorts, the independent Safety Monitoring Committee of the Phase 1 clinical trial endorsed continued dose exploration by proceeding to the last planned cohort. Doses of 7 mg/kg or 10 mg/kg of suvodirsen were administered to two patients in the fifth cohort and were associated with similar adverse events as those observed at lower doses but were more severe in intensity. The full data from the Phase 1 clinical trial will be presented in an oral presentation and poster at today's MDA conference.

"The safety profile of suvodirsen observed in this study is encouraging and supports continued progression to a Phase 2/3 study," said Kathryn Wagner, MD, PhD, chair of the suvodirsen clinical advisory committee and director of the Center for Genetic Muscle Disorders at the Kennedy Krieger Institute at the Johns Hopkins School of Medicine. "These data, along with Wave's innovative approach to chemical design and clinical development, make me optimistic about suvodirsen's potential as a possible DMD treatment."

Design for Phase 2/3 DYSTANCE 51 Clinical Trial

In a second poster, Wave will present the design of DYSTANCE 51, a global, multicenter, randomized, double-blind, placebo-controlled Phase 2/3 efficacy and safety clinical trial of suvodirsen in DMD patients amenable to exon 51 skipping. This clinical trial is designed to enroll boys who are between 5 and 12 years of age (inclusive) with a genetically confirmed diagnosis of DMD amenable to exon 51 skipping therapy. Patients will be randomized to receive 4.5 mg/kg or 3 mg/kg of suvodirsen or placebo administered intravenously once weekly for 48 weeks. The 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. Both doses have been selected based on the Phase 1 clinical trial results as well as data from *in vitro* and *in vivo* nonclinical studies

The DYSTANCE 51 primary efficacy endpoints will measure change in dystrophin protein level and change in the North Star Ambulatory Assessment score. In addition, this Phase 2/3 clinical trial will include multiple functional outcome measures as secondary efficacy endpoints. DYSTANCE 51 is expected to be initiated in July 2019 and the company intends to use the results of this trial to seek regulatory approvals globally.

Earlier this year, Wave announced that the DYSTANCE 51 clinical trial was selected for the U.S. Food and Drug Administration (FDA) pilot program for complex innovative trial designs. As a participant in the pilot program, the company has additional opportunities to meet with FDA staff to discuss the design elements of the trial, including the potential use of Bayesian methods to adapt the trial with the aim of allowing for more efficient and productive clinical determinations.

Ongoing Open-label Extension Study

Suvodirsen is currently being studied in an ongoing, multi-dose, open-label extension (OLE) study initiated in August 2018 with patients from the Phase 1 clinical trial. The company expects to report an interim analysis of dystrophin expression from muscle biopsies in boys receiving suvodirsen in the OLE study in the second half of 2019. Data from this analysis are intended to serve as an important component of a submission to the FDA for accelerated approval.

Investor Conference Call and Webcast

Wave management will host an investor webcast and conference call today at 7:30 a.m. ET to discuss the Phase 1 safety and tolerability results of suvodirsen, as well the design of the DYSTANCE 51 Phase 2/3 clinical trial. The conference call may be accessed by dialing (866) 220-8068 for participants based in the United States. or +1 (470) 495-9153 for participants based outside the United States and entering conference ID 8975967. The accompanying slide presentation and live webcast may be accessed by visiting the investor relations section of the Wave Life Science corporate website at www.ir.wavelifesciences.com. Following the webcast, a replay will be available on the website.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a fatal X-linked genetic neuromuscular disorder caused predominantly by out-of-frame deletions in the *dystrophin* gene, resulting in absent or defective dystrophin protein. Dystrophin protein is needed for normal muscle maintenance and operation. Because of the genetic mutations in DMD, the body cannot produce functional dystrophin, which results in progressive and irreversible loss of muscle function, including the heart and lungs. Worldwide, DMD affects approximately one in 5,000 newborn boys.

About Suvodirsen (WVE-210201)

Suvodirsen is an investigational stereopure oligonucleotide that has been shown to induce skipping of exon 51 of *dystrophin* pre-mRNA in preclinical studies and is intended for the treatment of Duchenne muscular dystrophy (DMD). Approximately 13% of DMD patients have genetic mutations that are amenable to treatment with an exon 51 skipping therapy. Exon-skipping technology has the potential to induce cellular machinery to 'skip over' a targeted exon and restore the reading frame, resulting in the production of internally truncated, but functional dystrophin protein. Wave preclinical *in vitro* experiments using gymnotic delivery (free uptake) of suvodirsen in DMD patient-derived myoblasts demonstrated efficient exon 51 skipping and dystrophin protein restoration. Preclinical Western blot studies of suvodirsen demonstrated 52% dystrophin protein restoration compared with normal skeletal muscle tissue lysates. Suvodirsen has been granted orphan drug designation for the treatment of DMD by the U.S. Food and Drug Administration (FDA) and the European Commission, as well as rare pediatric disease designation by the FDA. In addition, the planned Phase 2/3 clinical trial of suvodirsen, DYSTANCE 51, was the first study ever selected for the FDA pilot program for complex innovative trial designs (CID).

About Wave Life Sciences

Wave Life Sciences (NASDAQ: WVE) 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. To find out more, please visit www.wavelifesciences.com and follow Wave on Twitter @WaveLifeSci.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, the planned presentation today of the final results from the Phase 1 clinical trial of suvodirsen in DMD, the expected timing of initiation of the Phase 2/3 clinical trial for suvodirsen in DMD, the plans to report interim efficacy data from the ongoing open-label extension study with patients from the Phase 1 clinical trial of suvodirsen in DMD, the belief that the safety and tolerability data from the Phase 1 clinical trial supports initiation of a Phase 2/3 clinical trial, Wave's intention to use the results of the Phase 2/3 trial to seek regulatory approvals, Wave's plans and expectations regarding the design of the Phase 2/3 clinical trial, and Wave's expectations regarding the selection of the Phase 2/3 trial for the FDA pilot program for complex innovative trial design. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from

those expressed or implied by any forward-looking statements contained in this press release. These risks and uncertainties include but are not limited to the following: Wave's current and planned clinical trials, other studies for suvodirsen, and Wave's other product candidates may not be successful or may take longer and be more costly than anticipated; product candidates that appeared promising in earlier research and clinical trials may not demonstrate safety and/or efficacy in later-stage or larger-scale clinical trials; and the other risk factors discussed under the heading "Risk Factors" contained in Wave's Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission (SEC), as well as in other filings Wave makes with the SEC from time to time. All statements contained in this press release are made only as of the date of this press release, and Wave undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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Exhibit 99.2

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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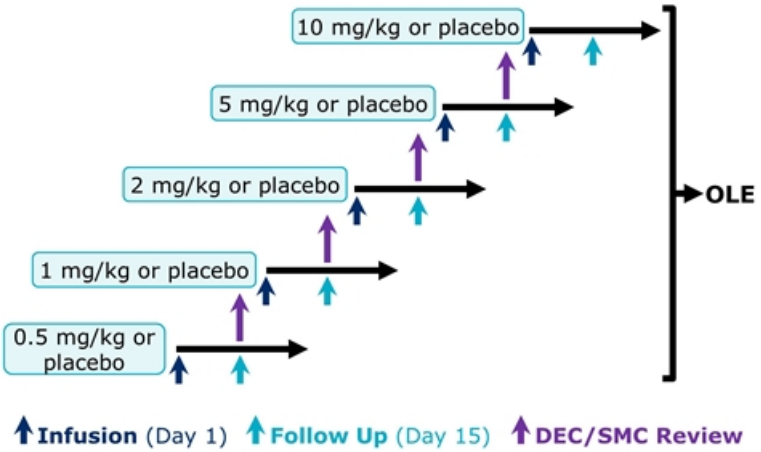
Study Design

- 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

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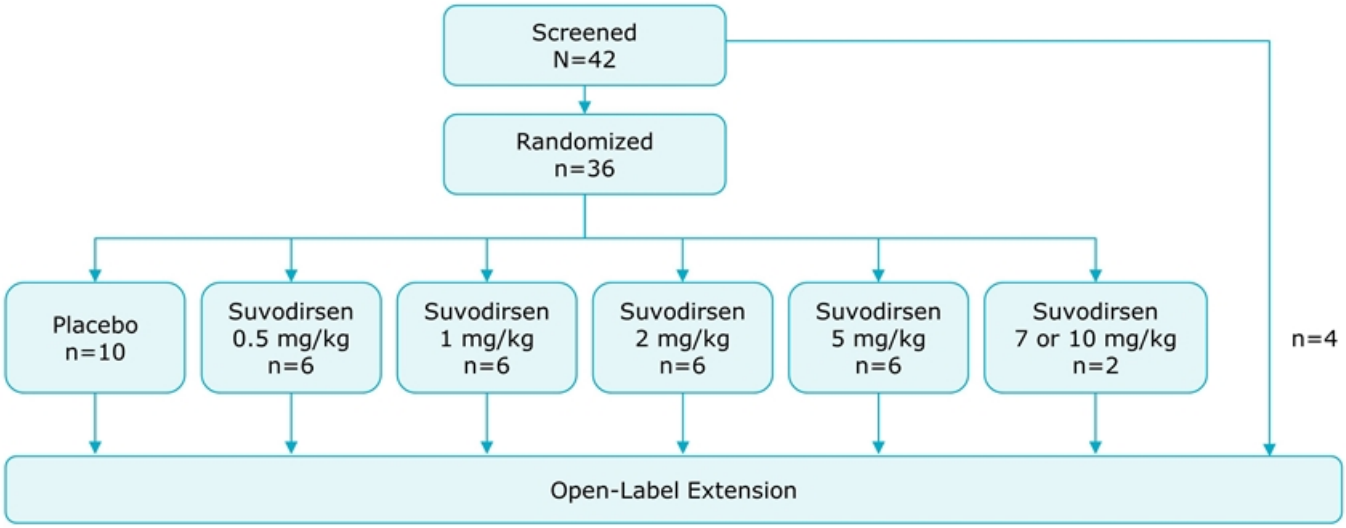
AE=adverse event; PK=pharmacokinetic; SAE=serious AE.

Patient Disposition



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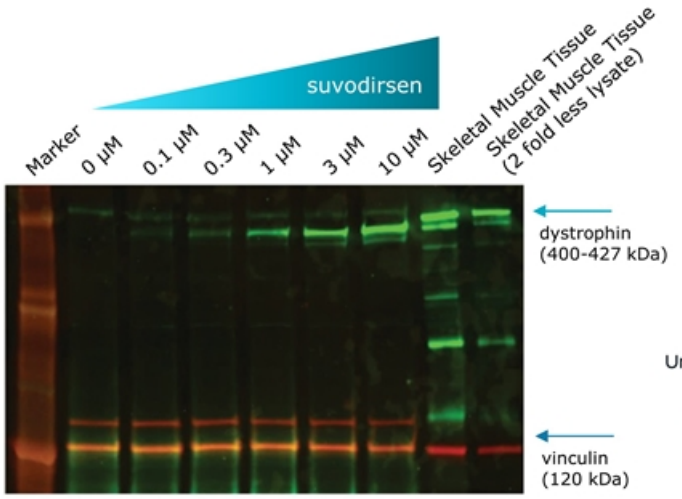
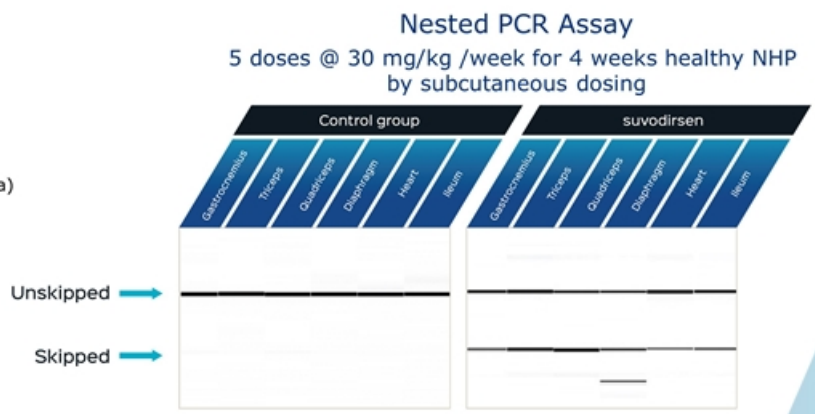
DYSTANCE 51: A Phase 2/3 Clinical Trial of Suvodirsen in Patients with Duchenne Muscular Dystrophy

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





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

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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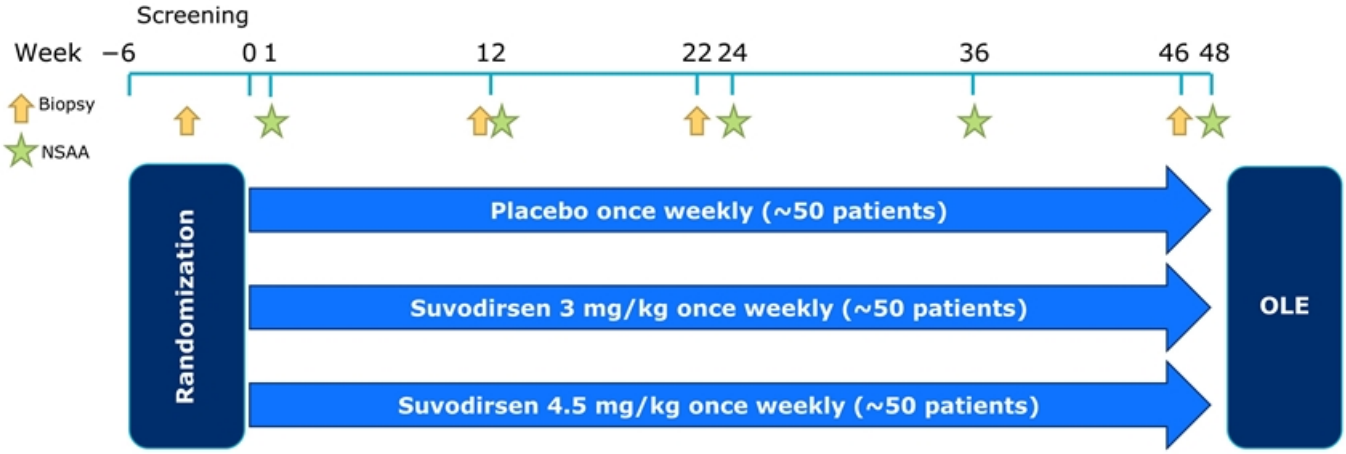
DYSTANCE 51 Phase 2/3 Trial Study Design



- 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

WAVE LIFE SCIENCES

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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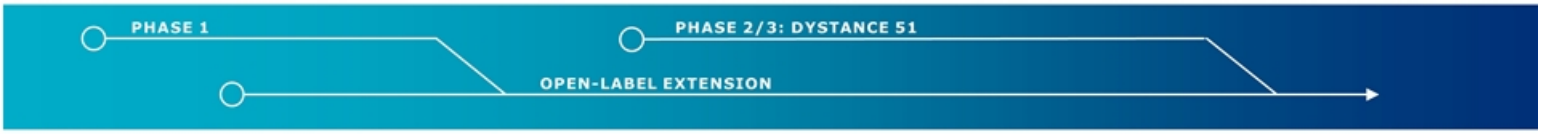
AE=adverse event; DMD=Duchenne muscular dystrophy; hsCRP=high-sensitivity C-reactive protein; IAR=infusion-associated reaction
Note: 4.5 mg/kg dose in DYSTANCE 51 provides approximately the same amount of active ingredient as the 5 mg/kg dose in the Phase 1 clinical trial

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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Wave Life Sciences
Muscular Dystrophy Association
Clinical and Scientific Conference
Investor Update
April 16, 2019