
**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): December 19, 2022

WAVE LIFE SCIENCES LTD.

(Exact name of registrant as specified in its charter)

Singapore
(State or other jurisdiction
of incorporation)

001-37627
(Commission
File Number)

00-000000
(IRS Employer
Identification No.)

**7 Straits View #12-00, Marina One
East Tower
Singapore**
(Address of principal executive offices)

018936
(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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
\$0 Par Value Ordinary Shares	WVE	The Nasdaq Global Market

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 December 19, 2022, Wave Life Sciences Ltd. (the “Company” or “Wave”) issued a press release announcing a positive update from the initial cohort of the Phase 1b/2a proof-of-concept study of WVE-N531, the Company’s exon 53 exon-skipping oligonucleotide for the treatment of Duchenne muscular dystrophy (“DMD”). High muscle concentrations of WVE-N531 and exon skipping were observed six weeks after initiating biweekly multidosing with 10 mgs/kg, achieving proof-of-concept in the study. WVE-N531 also appeared safe and well-tolerated. The initial cohort is an open-label, intra-patient dose escalation clinical trial evaluating WVE-N531 as a treatment for boys with DMD who are amenable to exon 53 skipping. A copy of the press release is attached hereto as Exhibit 99.1 and incorporated by reference herein.

The press release also indicated that Wave management will host an investor conference call at 8:30 a.m. ET on December 19, 2022 to discuss these results. For purposes of the call, and in connection with the announcement described above, the Company plans to share an investor slide presentation during the investor conference call, which will be available on the “For Investors & Media” section of the Company’s website at <http://ir.wavelifesciences.com/>.

The information in this Item 7.01 is being furnished 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 it be deemed incorporated by reference into any registration statement or other 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.

Item 8.01 Other Events.

The information set forth in the press release referred to in Item 7.01 above, other than the second, third 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

The following exhibit relating to Item 7.01 is furnished and not filed:

Exhibit No.	Description
99.1	Press Release issued by Wave Life Sciences Ltd. dated December 19, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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/ Paul B. Bolno, M.D.

Paul B. Bolno, M.D.

President and Chief Executive Officer

Date: December 19, 2022



Wave Life Sciences Provides Positive Update on Proof-of-Concept Study for WVE-N531 in Duchenne Muscular Dystrophy

53% mean exon skipping and <1% (BLQ) mean dystrophin expression six weeks after initiating biweekly multidosing

PN chemistry improved pharmacology of WVE-N531 compared with Wave's first-generation DMD program – demonstrated high muscle concentrations with a mean of 42 micrograms/gram

WVE-N531 appeared safe and well tolerated

Third Wave clinical trial evaluating a PN chemistry-containing compound to achieve target engagement in 2022

Wave to host investor conference call and webcast at 8:30 a.m. ET today

CAMBRIDGE, Mass., December 19, 2022 – Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage genetic medicines company committed to delivering life-changing treatments for people battling devastating diseases, announced today a positive update from the initial cohort of the Phase 1b/2a proof-of-concept study of WVE-N531 in three boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. High muscle concentrations of WVE-N531 and exon skipping were observed six weeks after initiating biweekly multidosing with 10 mgs/kg, achieving proof-of-concept in the study. WVE-N531 also appeared safe and well-tolerated.

“These data provide early evidence that WVE-N531 is working as intended, leading to substantial exon skipping after just three consecutive doses. This is the earliest timepoint at which exon skipping has been reported in a clinical trial of boys with DMD,” said Anne-Marie Li-Kwai-Cheung, Chief Development Officer of Wave Life Sciences. “While dystrophin was below the lower limit of detection, it is expected that dystrophin protein production would lag splicing of the RNA transcript. We are encouraged by these early results and are evaluating next steps for the program, including the continuation of this initial cohort. We would like to express our sincerest gratitude to the boys, their families, and the investigators who participated in the study.”

“There remains a significant unmet need in DMD for new treatment options. It is exciting to see this level of exon skipping in a short period of time, especially since skipping would be expected to increase over a longer dosing interval,” said Laurent Servais, MD, PhD, professor of pediatric neuromuscular diseases at the MDUK Oxford Neuromuscular Center and primary investigator in the WVE-N531 study. “Based on the data, it appears Wave’s next-generation chemistry has led to significantly improved pharmacology. Expression of dystrophin after longer exposure will, of course, be key to confirm the promise of these early data. I look forward to the continued progression of clinical research for WVE-N531.”

Three ambulatory boys participated in this open-label, intra-patient dose escalation clinical trial ([NCT04906460](#)). The boys received single escalating doses of 1, 3, 6 and 10 mg/kg; and in the multidose portion of the study, the same boys received three doses of 10 mg/kg every other week. A muscle biopsy was taken two weeks after the third and final dose, which was six weeks after the first dose.

Results included:

- WVE-N531 resulted in a mean tissue concentration of 42 micrograms/gram (6.1 micromolar)
- RNAscope results indicate WVE-N531 is reaching the nucleus in muscle cells
- WVE-N531 resulted in mean exon skipping of 53% (range: 48-62%) as measured by RT-PCR
- Mean dystrophin production was 0.27% of normal as measured by Western blot, which was below the level of quantification (BLQ: 1%)
- Plasma concentrations following a single dose of 10 mg/kg support potential to move from biweekly to monthly dosing
- Adverse events were all mild, except for a COVID-19 infection of moderate intensity. There were no serious adverse events, no trends in labs, and no oligonucleotide class-related safety events.

“These data indicate PN chemistry can improve potency, distribution and durability of splicing oligonucleotides without needing peptide or antibody conjugates, clearly indicating the increasing potential of Wave’s PRISM platform,” said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. “This is Wave’s third clinical trial in 2022 to demonstrate the impact of PN chemistry, as well as our third clinical trial to demonstrate translation of preclinical data in humans. In 2023, we are looking forward to determining next steps for WVE-N531, advancing our silencing clinical programs, and bringing a whole new modality into the clinic with our RNA editing and upregulation capability.”

Investor Conference Call and Webcast

Wave management will host an investor conference call today at 8:30 a.m. ET to discuss results from this WVE-N531 proof-of-concept study. The webcast of the conference call and corresponding slide presentation may be accessed by visiting “Events” on the investor relations section of the Wave Life Sciences corporate website: ir.wavelifesciences.com/events-and-presentations.

Analysts planning to participate during the Q&A portion of the live call can join the conference call at the audio conferencing link available [here](#). Once registered, participants will receive the dial-in information. Following the live event, an archived version of the webcast will be available on the Wave Life Sciences 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. Approximately 8%-10% of boys with DMD have mutations amenable to treatment with an exon 53 skipping therapy. Exon skipping aims to address the underlying cause of DMD by promoting the production of dystrophin protein to stabilize or slow disease progression.

About PRISM™

PRISM is Wave Life Sciences’ proprietary discovery and drug development platform that enables genetically defined diseases to be targeted with stereopure oligonucleotides across multiple therapeutic modalities, including silencing, splicing and editing. PRISM combines the company’s unique ability to construct stereopure oligonucleotides with a deep understanding of how the interplay among oligonucleotide sequence, chemistry and backbone stereochemistry impacts key pharmacological properties. By exploring these interactions through iterative analysis of *in vitro* and *in vivo* outcomes and machine learning-driven predictive modeling, the company continues to define design principles that are deployed across programs to rapidly develop and manufacture clinical candidates that meet pre-defined product profiles.

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](https://twitter.com/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, our understanding of the anticipated therapeutic benefit of WVE-N531 as a therapy for DMD; our understanding of the cause of DMD and the potential addressable patients amenable to treatment with an exon 53 skipping therapy; our expectations that the level of exon skipping would be expected to increase over a longer dosing interval; our expectation that dystrophin protein production would lag splicing of the RNA transcript; our beliefs regarding the learnings gained from our first-generation DMD program; our expectation regarding the continued progression of clinical research for WVE-N531; and the potential benefits of PRISM, including our novel PN backbone chemistry modifications, and our stereopure oligonucleotides compared with stereorandom oligonucleotides. 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 and actual results may differ materially from those indicated by these forward-looking statements as a result of these risks, uncertainties and important factors, including, without limitation, the risks and uncertainties described in the section entitled "Risk Factors" in Wave's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as amended, and in other filings Wave makes with the SEC from time to time. Wave undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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