



Wave Life Sciences Reports Third Quarter 2022 Financial Results and Provides Business Update

November 10, 2022

Announced positive update in third quarter from SELECT-HD trial in HD; single doses of WVE-003 appeared generally safe and well-tolerated and suggested allele-selective reduction of mHTT protein in CSF

Multidosing underway in Phase 1b/2a trial of WVE-N531 in boys with DMD amenable to exon 53 skipping; muscle biopsy data from initial cohort on track for 4Q 2022

Selected WVE-006 (Wave's first RNA editing candidate) as development candidate for AATD with CTA submissions expected in 2023

Preclinical data presentations at OTS and ESGCT meetings highlighted potential of PRISM platform to develop potent and durable siRNA compounds and unlock new biology with AIMers

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

CAMBRIDGE, Mass., Nov. 10, 2022 (GLOBE NEWSWIRE) -- 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 financial results for the third quarter ended September 30, 2022 and provided a business update.

"In the third quarter, we continued to deliver on our key milestones for 2022, including announcing a positive update from our Huntington's disease trial and selecting our first-in-class RNA editing candidate for alpha-1 antitrypsin deficiency," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Clinical data emerging from our pipeline supports the translational potential of our unique PRISM platform and we look forward to sharing a third data update this quarter with the first muscle biopsy data from our Phase 1b/2a clinical trial of WVE-N531 for Duchenne muscular dystrophy. Additionally, we believe that our RNA editing capability using endogenous ADAR enzymes provides a unique opportunity for Wave and we are well-positioned to be leaders in the editing field. We are working toward bringing RNA editing to the clinic and are on track to submit clinical trial applications for our alpha-1 antitrypsin deficiency program in 2023."

Recent Pipeline and Business Highlights

SELECT-HD clinical trial for WVE-003 in Huntington's disease (HD) continues to advance; only allele-selective clinical program designed to reduce mutant HTT and spare healthy HTT

- WVE-003 (PN-modified allele-selective silencing oligonucleotide) for HD is being evaluated in the ongoing, adaptive, double-blind Phase 1b/2a SELECT-HD clinical trial ([NCT05032196](#)). WVE-003 is the only compound in clinical development designed to selectively lower mutant huntingtin (mHTT) protein levels, while leaving wild-type (healthy) huntingtin (wtHTT) protein levels relatively intact.
- In September 2022, Wave announced a positive update from the company's ongoing SELECT-HD clinical trial driven by the observation of reductions in mHTT protein in cerebrospinal fluid (CSF) after study participants received either a single 30 or 60 mg dose of WVE-003. Additionally, wtHTT protein was preserved, which appeared consistent with allele-selectivity. Single doses of WVE-003 appeared generally safe and well-tolerated.
- Based on the SELECT-HD data, Wave is adapting the trial to expand the single dose cohorts, including in a 90 mg single dose cohort for which biomarker data were not available at the time of analysis. Wave expects to share additional single-dose biomarker and safety data in the first half of 2023.
- In November 2022, these SELECT-HD data were presented in an oral presentation at the Huntington Study Group (HSG) Annual Meeting in Tampa, Florida.

Phase 1b/2a clinical trial of WVE-N531 in Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping continues to advance; multi-dosing is underway at human-equivalent levels in the range explored in preclinical double-knockout (dKO) mouse

- WVE-N531 (PN-modified splicing oligonucleotide) for DMD is being evaluated in an open-label, intra-patient dose escalation clinical trial ([NCT04906460](#)). Dose escalation is complete and multi-dosing is underway with three 10 mg/kg doses of WVE-N531 every other week, to be followed by planned muscle biopsies. Clinical biomarker and safety data is expected in the fourth quarter of 2022. Possible cohort expansion will be informed by an assessment of the concentration and distribution of WVE-N531 in muscle tissue, as well as biomarkers, including exon skipping and dystrophin.
- Plasma concentrations and half-life of WVE-N531 observed in patients receiving 10 mg/kg of WVE-N531 in Wave's ongoing clinical trial were significantly greater than plasma concentrations achieved following the highest doses of suvodirsen, Wave's first-generation PS/PO exon skipping compound administered in a Phase 2/3 study. This pharmacokinetic analysis suggests the potential for significantly improved pharmacologic properties of WVE-N531, including distribution and stability in muscle.

FOCUS-C9 clinical trial of WVE-004 for C9orf72-associated amyotrophic lateral sclerosis and frontotemporal dementia (C9-ALS and C9-FTD) continues to advance; open-label extension trial recently initiated

- FOCUS-C9 ([NCT04931862](#)) is an adaptive Phase 1b/2a clinical trial that is designed to rapidly optimize dose level and frequency based on early indicators of target engagement. WVE-004 is designed to selectively target transcript variants

containing a hexanucleotide repeat expansion (G₄C₂) associated with the C9orf72 gene for the treatment of C9-ALS and C9-FTD, thereby reducing pathological mRNA products and toxic DPR proteins, including poly(GP).

- Based on potency and durability of pharmacodynamic effects, the multidose portion of the FOCUS-C9 trial was expanded to evaluate quarterly dosing. Data from all cohorts in the FOCUS-C9 clinical trial are expected in the first half of 2023.
- In November 2022, Wave presented previously disclosed clinical data from the ongoing FOCUS-C9 clinical trial at the International Society for Frontotemporal Dementias in Lille, France.
- An open-label extension trial for participants in the FOCUS-C9 trial was initiated in the fourth quarter of 2022.

Alpha-1 antitrypsin deficiency (AATD) development candidate (WVE-006) designed to correct mutant AATD transcript to address both liver and lung manifestations of disease highlighted at virtual event

- In the third quarter, Wave selected WVE-006 (PN-modified GalNAc-conjugated development candidate) as its development candidate for the treatment of AATD. In September 2022, Wave highlighted WVE-006 in a virtual event, "Towards the Clinic: Spotlight on RNA Editing for AATD." The event replay is available [here](#). WVE-006 is Wave's first AIMer (A-to-I(G) RNA base editing oligonucleotide) development candidate. WVE-006 is first-in-class in AATD and is the most advanced program currently in development using an oligonucleotide to harness an endogenous enzyme for editing.
- In October 2022, preclinical data for WVE-006 was highlighted in an oral presentation at the 18th Annual Meeting of the Oligonucleotide Therapeutics Society (OTS). The meeting represented the first presentation in a scientific congress of preclinical data supporting WVE-006 as a potential best-in-class therapeutic approach in AATD. The OTS presentation slides are available [here](#).

PRISM platform: RNA editing and small interfering RNA (siRNA) capabilities highlighted across six presentations and posters at recent scientific congresses

- Wave's preclinical-stage siRNA designs, which incorporate PRISM chemistry, were highlighted at the OTS Meeting in October 2022. The OTS poster is available [here](#). The data demonstrated remarkably robust and durable RNA silencing *in vivo* in mice, further illustrating the evolution and the potential of Wave's chemistry.
- Wave's application of ADAR-mediated RNA editing to modulate protein-protein interactions in mice was also highlighted in a poster accepted at the European Society of Gene and Cell Therapy (ESGCT) meeting in October 2022. The ESGCT poster is available [here](#).

Key Anticipated Upcoming Milestones

WVE-003 for HD:

- Additional single-dose biomarker and safety clinical data expected in 1H 2023.

WVE-N531 for DMD:

- Clinical data, including muscle biopsies, expected in 4Q 2022 to provide further insight into the clinical effects of PN chemistry and enable decision-making for this program.

WVE-004 for C9-ALS and C9-FTD:

- Clinical data from all cohorts in the FOCUS-C9 trial expected in 1H 2023.

WVE-006 (GalNAc-conjugated AIMer) for AATD:

- Wave expects to submit clinical trial applications (CTAs) in 2023.

Third Quarter 2022 Financial Results and Financial Guidance

Wave reported a net loss of \$39.0 million in the third quarter of 2022, as compared to \$6.2 million in the same period in 2021. Wave recorded revenue of \$0.3 million for the third quarter of 2022, as compared to \$36.4 million in the same period in 2021. The decrease in revenue year-over-year was primarily driven by the amendment to the Takeda Collaboration in the third quarter of 2021.

Research and development expenses were \$27.6 million in the third quarter of 2022 as compared to \$31.1 million in the same period in 2021. The decrease in research and development expenses in the third quarter was primarily due to decreased external expenses related to our HD programs and decreases in other research and development expenses, partially offset by increased external expenses related to C9 and our other clinical and preclinical programs.

General and administrative expenses were \$11.6 million in the third quarter of 2022 as compared to \$12.9 million in the same period in 2021. The decrease in general and administrative expenses in the third quarter of 2022 was primarily due to decreases in compensation-related expenses, as well as decreases in other external general and administrative expenses.

As of September 30, 2022, Wave had \$122.0 million in cash, cash equivalents and short-term investments. As of December 31, 2021, Wave had \$150.6 million in cash and cash equivalents. The decrease is primarily due to Wave's year to date operating cash burn, partially offset by \$65.5 million in net proceeds from its financing in June 2022.

Wave expects that its existing cash, cash equivalents and short-term investments will enable the company to fund its operating and capital expenditure requirements to the end of 2023.

Investor Conference Call and Webcast

Wave management will host an investor conference call today at 8:30 a.m. ET to discuss the third quarter 2022 financial results and provide a business update. A webcast of the conference call 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 following 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 the SELECT-HD Clinical Trial

The SELECT-HD trial is a global, multicenter, randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial to assess the safety and tolerability of single- and multiple-ascending intrathecal doses of WVE-003 in people with a confirmed diagnosis of HD who are in the early stages of the disease and carry SNP3 in association with their cytosine-adenine-guanine (CAG) expansion. Additional objectives include assessing the plasma pharmacokinetic profile and exposure in the cerebrospinal fluid, as well as exploratory pharmacodynamic (mHTT, wtHTT and neurofilament light chain) and clinical endpoints. It is designed to be adaptive, with dose escalation and dosing frequency being guided by an independent committee.

In an initial data analysis, single doses of WVE-003 up to 90 mg appeared generally safe and well-tolerated. Adverse events (AEs) were balanced across treatment groups, including placebo, and all were mild to moderate in intensity. No serious adverse events (SAEs) were observed and no participants discontinued from the study. Among participants in the 30 and 60 mg WVE-003 cohorts, the mean reduction in CSF mHTT from baseline was 22% (median reduction 30%) at 85 days following a single dose. The difference in the mean reduction in CSF mHTT compared to placebo was 35% at 85 days post-single dose. For these analyses, the 30 and 60 mg single dose cohorts were pooled as there was no apparent dose response between these two cohorts. Wave will continue to evaluate dose response in the expanded single dose cohorts. In the 30 and 60 mg cohorts, wtHTT protein was preserved, which appears consistent with allele-selectivity. Increases in neurofilament light chain (NfL) from baseline were observed in some participants. Wave will continue to monitor trends in NfL as SELECT-HD advances. There were no clinically meaningful elevations in CSF white blood cell counts or protein that would indicate inflammation in the CNS. There were no meaningful changes in clinical outcome measures, although the dataset and duration were not sufficient to assess clinical effects.

About the FOCUS-C9 Clinical Trial

The FOCUS-C9 trial is an ongoing, global, multicenter, randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial to assess the safety and tolerability of single- and multiple-ascending intrathecal doses of WVE-004 for people with C9-ALS and/or C9-FTD. Additional objectives include measurement of poly(GP) DPR proteins in the cerebrospinal fluid (CSF), plasma and CSF pharmacokinetics (PK), and exploratory biomarkers and clinical outcomes. The FOCUS-C9 trial is designed to be adaptive, with dose escalation and dosing frequency being guided by an independent committee.

In an initial data analysis, reductions in poly(GP) were observed across all active treatment groups (10 mg, n=2 patients; 30 mg, n=4 patients; 60 mg, n=3 patients), reaching statistical significance versus placebo (n=3 patients) after single 30 mg doses, with a 34% reduction in poly(GP) at day 85 (p=0.011). At the time of analysis, none of the patients dosed with 60 mg had reached day 85. As the poly(GP) reduction in the 30 mg single dose cohort does not appear to have plateaued, Wave will extend the observation period from approximately three months (85 days) to approximately six months to identify the maximum reduction of poly(GP) and duration of effect of low single doses. Based on the durability and potency observed in the 30 mg cohort, FOCUS-C9 has been adapted to include additional patients receiving 20 mg and 30 mg single doses of WVE-004. Adverse events (AEs) were balanced across treatment groups, including placebo, and were mostly mild to moderate in intensity. Four patients (including one on placebo) experienced severe and/or serious adverse events; three were reported by the investigators to be related to ALS or administration, and one was reported by the investigator to be related to study drug. There were no treatment-associated elevations in CSF white blood cell counts or protein and no other notable laboratory abnormalities were observed.

Support for FOCUS-C9 is provided by the Alzheimer's Drug Discovery Foundation.

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 concerning our goals, beliefs, expectations, strategies, objectives and plans, and other statements that are not necessarily based on historical facts, including statements regarding the following, among others: the anticipated initiation, site activation, patient recruitment, patient enrollment, dosing, generation of data and completion of our adaptive clinical trials, and the announcement of such events; the protocol, design and endpoints of our ongoing and future clinical trials; the future performance and results of our programs in clinical trials; future preclinical activities and programs; regulatory submissions; the progress and potential benefits of our collaborations with partners; the potential of our preclinical data to predict the behavior of our compounds in humans; our identification and expected timing of future product candidates and their therapeutic potential; the anticipated therapeutic benefits of our potential therapies compared to others; our ability to design compounds using multiple modalities and the anticipated benefits of that approach; the potential benefits of PRISM, including our novel PN backbone chemistry modifications, and our stereopure oligonucleotides compared with stereorandom oligonucleotides; the potential benefits of our novel ADAR-mediated RNA editing platform capabilities, including our AIMers, compared to others; the status and progress of our novel programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; the benefit of nucleic acid therapeutics generally; the strength of our intellectual property; our assumptions based on our balance sheet and the anticipated duration of our cash runway; our intended uses of capital; and our expectations regarding the impact of the COVID-19 pandemic on our business. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the following: our ability to finance our drug discovery and development efforts and to raise additional capital when needed; the ability of our preclinical programs to produce data sufficient to support our clinical trial applications and the timing thereof; the clinical results of our programs and the timing thereof, which may not support further development of product candidates; actions of regulatory agencies and their receptiveness to our adaptive trial designs, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing regulatory interactions and future clinical trials; the effectiveness of PRISM, including our novel PN backbone chemistry modifications; the effectiveness of our novel ADAR-mediated RNA editing platform capability and our AIMers; our ability to demonstrate the therapeutic benefits of our candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our dependence on third parties, including contract research organizations, contract manufacturing organizations, collaborators and partners; our ability to manufacture or contract with third parties to manufacture drug material to support our programs

and growth; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for similar indications; our ability to maintain the company infrastructure and personnel needed to achieve our goals; the severity and duration of the COVID-19 pandemic and variants thereof, and its negative impact on the conduct of, and the timing of enrollment, completion and reporting with respect to our clinical trials; and any other impacts on our business as a result of or related to the COVID-19 pandemic, as well as the information under the caption "Risk Factors" contained in our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and in other filings we make with the SEC from time to time. We undertake no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 96,954	\$ 150,564
Short-term investments	25,044	—
Prepaid expenses	7,419	6,584
Other current assets	2,017	5,416
Total current assets	131,434	162,564
Long-term assets:		
Property and equipment, net	18,552	22,266
Operating lease right-of-use assets	27,827	18,378
Restricted cash	3,654	3,651
Other assets	44	148
Total long-term assets	50,077	44,443
Total assets	\$ 181,511	\$ 207,007
Liabilities, Series A preferred shares and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 15,934	\$ 7,281
Accrued expenses and other current liabilities	11,056	14,861
Current portion of deferred revenue	32,341	37,098
Current portion of operating lease liability	4,928	4,961
Total current liabilities	64,259	64,201
Long-term liabilities:		
Deferred revenue, net of current portion	80,230	77,479
Operating lease liability, net of current portion	33,667	24,955
Total long-term liabilities	113,897	102,434
Total liabilities	\$ 178,156	\$ 166,635
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at September 30, 2022 and December 31, 2021	\$ 7,874	\$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 86,841,523 and 59,841,116 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	\$ 802,697	\$ 749,851
Additional paid-in capital	116,535	87,980
Accumulated other comprehensive income (loss)	(123)	181
Accumulated deficit	(923,628)	(805,514)
Total shareholders' equity (deficit)	\$ (4,519)	\$ 32,498
Total liabilities, Series A preferred shares and shareholders' equity (deficit)	\$ 181,511	\$ 207,007

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue	\$ 285	\$ 36,423	\$ 2,410	\$ 39,199
Operating expenses:				
Research and development	27,575	31,086	84,778	96,114
General and administrative	11,609	12,944	36,789	33,991
Total operating expenses	39,184	44,030	121,567	130,105
Loss from operations	(38,899)	(7,607)	(119,157)	(90,906)
Other income (expense), net:				
Dividend income and interest income, net	596	6	746	25

Other income (expense), net	(701)	1,371	297	3,421
Total other income (expense), net	(105)	1,377	1,043	3,446
Loss before income taxes	(39,004)	(6,230)	(118,114)	(87,460)
Income tax provision	—	—	—	—
Net loss	<u>\$ (39,004)</u>	<u>\$ (6,230)</u>	<u>\$ (118,114)</u>	<u>\$ (87,460)</u>
Net loss per share attributable to ordinary shareholders—basic and diluted	<u>\$ (0.42)</u>	<u>\$ (0.12)</u>	<u>\$ (1.60)</u>	<u>\$ (1.75)</u>
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	<u>93,900,484</u>	<u>50,709,877</u>	<u>73,754,417</u>	<u>50,017,521</u>
Other comprehensive loss:				
Net loss	\$ (39,004)	\$ (6,230)	\$ (118,114)	\$ (87,460)
Foreign currency translation	(76)	(11)	(304)	(131)
Comprehensive loss	<u>\$ (39,080)</u>	<u>\$ (6,241)</u>	<u>\$ (118,418)</u>	<u>\$ (87,591)</u>

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