Wave Life Sciences Reports Fourth Quarter and Full Year 2022 Financial Results and Provides Business Update

March 22, 2023

Achieved clinical validation of PRISM platform in 2022 – demonstrated ability to potently and durably engage RNA targets and translate preclinical data to the clinic

Extended leadership in RNA editing and advanced WVE-006 for AATD – first-in-class RNA editing candidate transitioning to clinical development in 2023

Initiating Part B of WVE-N531 study in exon 53-amenable DMD to assess dystrophin after 24 and 48 weeks of biweekly dosing

Strategic collaboration with GSK underway, expected to add multiple first-in-class discovery programs to Wave pipeline, including RNA editing and RNAi programs, as well as potential for up to $3.3 billion in milestone payments

Well-capitalized with cash runway into 2025 to deliver on multiple catalysts

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

CAMBRIDGE, Mass., March 22, 2023 (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 fourth quarter and full year ended December 31, 2022 and provided a business update.

“2022 was a transformational year that positioned Wave to become the leading RNA medicines company. We achieved clinical validation of our PRISM platform, demonstrating target engagement in all three of our clinical programs and translation of our preclinical data to the clinic. We maintained our leadership in RNA editing by achieving the first RNA editing clinical candidate, WVE-006, which is a potentially comprehensive approach for treating alpha-1 antitrypsin deficiency. In December 2022, we entered into a strategic collaboration with GSK that we expect will continue to grow our pipeline with first-in-class candidates, further unlock our RNA editing and other platform capabilities, maximize commercial potential for WVE-006, and bring additional cash onto our balance sheet through research funding and potential collaboration milestones,” said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences.

“In 2023, we are poised to deliver the first RNA editing candidate to the clinic, which will be an exciting moment not just for Wave, but for the entire nucleic acids field. We are initiating Part B of the WVE-N531 study in Duchenne muscular dystrophy to assess dystrophin after 24 and 48 weeks of biweekly dosing, with potential for this program to become a significant commercial opportunity for Wave. We’re also on track for new clinical data from our HD and ALS/FTD programs. Beyond our ongoing clinical activities, we are driving forward the next wave of first- or best-in-class programs that expand our pipeline, and we expect to announce new wholly owned RNA editing programs and preclinical data this year.”

Recent Business Highlights

Established strategic collaboration with GSK with potential to drive substantial value for Wave

- In December 2022, Wave and GSK entered into a collaboration that will enable both companies to advance transformative oligonucleotide therapeutics. The collaboration provides multiple value drivers to Wave including:
  - **Maximizes commercial opportunities for WVE-006 for alpha-1 antitrypsin deficiency (AATD)**: GSK, which is a global leader in clinical development and commercialization, received the exclusive global license for Wave’s preclinical program for AATD called WVE-006, which uses proprietary “AIMer” technology (A-to-I(G) RNA base editing). Development and commercialization responsibilities will transfer to GSK after Wave completes the first-in-patient study.
  - **Expands pipeline and unlocks additional PRISM capabilities and modalities:** The agreement includes a discovery collaboration which enables Wave to advance up to three programs and GSK to advance up to eight programs, leveraging Wave’s PRISM platform and editing, splicing and silencing (RNAi and antisense) modalities, as well as GSK’s expertise and insights in genetics and genomics.
  - **Strengthens Wave’s financial position** : Wave received an upfront payment of $170 million, which included a cash payment of $120 million and a $50 million equity investment and will also receive research funding. Wave is eligible for up to $3.3 billion in potential milestone payments, including near-term preclinical and clinical milestones, as well as royalties, for WVE-006 and GSK’s eight collaboration programs.

Continued to expand versatile RNA medicines platform capabilities, including siRNA, to grow high-value and differentiated pipeline; new discovery programs to be disclosed in 2023, leading with RNA editing

- Wave is conducting discovery research across multiple modalities in both rare and prevalent indications, with the goal of

announcing updates, including preclinical data, on new hepatic discovery programs using GalNAc delivery in 2023.

- Wave continues to build out RNA editing capabilities beyond correction of single base mutations to expand target space and addressable patient populations. Beyond demonstrating last year that Wave's GalNAc AIMers are able to disrupt protein-protein interactions in the livers of mice, Wave also demonstrated that GalNAc-AIMers can edit RNA motifs to restore or upregulate gene expression in the livers of mice.
- Upregulation with AIMers provides a novel approach to endogenous mRNA delivery. Instead of giving exogenous mRNA therapies, AIMers can increase the expression of mRNA inside the cell. This means that, rather than correcting each mutation associated with a genetic disease one-by-one, upregulation with AIMers can restore healthy levels of proteins independent of genetic mutations, thereby significantly increasing the total addressable market.
- Wave also continues to advance preclinical research using siRNA oligonucleotides optimized with PRISM chemistry, with *in vivo* data demonstrating remarkably robust and durable silencing in mice using GalNAc conjugated siRNAs. Today, Wave announced data from its first *in vivo* siRNA study in the central nervous system (CNS), where Wave's unconjugated siRNA constructs demonstrated 70-90% APP silencing across six brain regions in mouse CNS at eight weeks, following a single intracerebroventricular (ICV) dose.

Advanced WVE-006, Wave's AATD development candidate, which is on track to become the first investigational RNA editing therapeutic to enter clinical development

- IND enabling studies for WVE-006 are underway and Wave is on track to submit clinical trial applications (CTAs) in the second half of 2023.
- WVE-006 is Wave's first AIMer development candidate. It is also first-in-class in AATD and is designed to correct mutant SERPINA1 transcript to address both liver and lung manifestations of the disease.

Achieved proof-of-concept in Part A of Phase 1b/2a clinical trial of WVE-N531 in Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping; initiating Part B (Phase 2) to assess dystrophin protein restoration

- In December 2022 (data cut-off: December 6, 2022), Wave reported positive data from the initial cohort of the proof-of-concept open-label study for WVE-N531 (splicing oligonucleotide), driven by the observation of high muscle concentrations of WVE-N531 (mean of 42 micrograms/gram) and exon skipping (mean of 53% as measured by RT-PCR) six weeks after initiating biweekly dosing at 10 mg/kg. Additionally, WVE-N531 appeared safe and well-tolerated.
- To evaluate dystrophin protein restoration, Wave plans to initiate Part B of the open-label study to enroll up to ten boys. Boys will be dosed at 10 mg/kg biweekly, and Wave plans to assess dystrophin protein after 24 and 48 weeks of biweekly dosing. The primary endpoint will be dystrophin protein levels, and the study will also evaluate safety and tolerability, pharmacokinetics, and functional endpoints. Data are expected in 2024.
- Today at 1:30 p.m. CT, Michael Tillinger, MD, Vice President of Clinical Development at Wave, will present an overview of the WVE-N531 data from December 2022, as well as next steps for the program, at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference.

Advanced CNS silencing clinical candidates, including delivery of first allele-selective target engagement data for WVE-003 in Huntington's disease (HD)

- In September 2022 (data cut-off: August 29, 2022), Wave announced a positive update from the Phase 1b/2a SELECT-HD trial of WVE-003 (allele-selective silencing oligonucleotide), driven by the observation of reductions in mutant huntingtin (mHTT) protein in cerebrospinal fluid after study participants received a single 30 mg or 60 mg dose of WVE-003. Additionally, wild-type huntingtin (wtHTT) protein was preserved, which appears consistent with allele-selectivity. WVE-003 was generally safe and well-tolerated.
- Based on the WVE-003 data, Wave adapted the SELECT-HD trial to expand the single dose cohorts to better define the treatment effect and decide on optimal doses for the multidose phase of the study. Wave expects to share additional single-dose biomarker and safety data from the 30, 60 and 90 mg cohorts in the first half of 2023.
- Additionally, the FOCUS-C9 Phase 1b/2a clinical trial of WVE-004 (silencing oligonucleotide) continues to advance, and Wave has completed recruitment for the ongoing multidose cohorts. Wave expects to share additional single and multidose data in the first half of 2023, including from the 10 mg monthly and 10 mg quarterly multidose cohorts.
- Both WVE-003 and WVE-004 are part of an active collaboration with Takeda, whereby Takeda has an option to co-develop and co-commercialize these candidates under a global 50:50 profit-split.

Key Anticipated Upcoming Milestones

WVE-N531 for DMD:

- Initiate dosing in Part B of WVE-N531 clinical trial in 2023
- Deliver data from Part B in 2024

WVE-006 for AATD:

- Submit CTAs for first-in-human study in 2H 2023

WVE-003 for HD:

- Deliver additional single-dose biomarker and safety clinical data in 1H 2023

WVE-004 for ALS/FTD:

- Deliver additional single- and multi-dose biomarker and safety clinical data in 1H 2023

Platform and Pipeline:

- Announce new wholly owned programs with preclinical data in 2023
- Advance collaboration activities with GSK, with potential for additional cash inflows in 2023 and beyond

Fourth Quarter and Full Year 2022 Financial Results and Financial Guidance

Wave reported a net loss of $43.7 million in the fourth quarter of 2022, as compared to $34.8 million in the same period in 2021. The increase in net loss in the fourth quarter from 2021 to 2022 was primarily driven by the increased spend on our clinical programs as well as increased compensation-related expenses, as discussed below. Wave reported a net loss of $161.8 million for the year ended December 31, 2022, as compared to $122.2 million for the year ended December 31, 2021. The increase in net loss year-over-year was primarily driven by the decrease in revenue recognized under the Takeda Collaboration.

Revenue earned under the Takeda Collaboration in the fourth quarter of 2022 was $1.2 million, as compared to $1.8 million in the same period in 2021. During the year ended December 31, 2022, Wave earned $3.6 million under the Takeda Collaboration, as compared to $41.0 million during the year ended December 31, 2021. The year-over-year decrease is primarily driven by the recognition of revenue related to the Takeda Amendment in the prior year period.

Research and development expenses were $31.1 million in the fourth quarter of 2022 as compared to $25.8 million in the same period in 2021. The increase in research and development expenses in the fourth quarter was primarily due to increased external expenses related to our AATD, C9orf72 and DMD programs and compensation-related costs, partially offset by a decrease in spending on our HD programs. Research and development expenses were $115.9 million in 2022, as compared to $121.9 million in 2021 primarily due to the previously disclosed discontinued PRECISION-HD programs, partially offset by increased spend on our other programs.

General and administrative expenses were $13.7 million in the fourth quarter of 2022 as compared to $12.1 million in the same period in 2021, primarily due to increases in professional and service fee expenses. General and administrative expenses were $50.5 million in 2022, as compared to $46.1 million in 2021. The increase in general and administrative expenses year-over-year was primarily due to increases in compensation-related expenses, as well as increases in other external general and administrative expenses.

As of December 31, 2022, Wave had $88.5 million in cash and cash equivalents, as compared to $150.6 million as of December 31, 2021. As previously disclosed, Wave entered into a strategic collaboration with GSK that became effective in the first quarter of 2023 and provided upfront cash of $170 million to Wave. Accordingly, the Company expects that its current cash and cash equivalents will be sufficient to fund operations into 2025.

Investor Conference Call and Webcast
Wave management will host an investor conference call today at 8:30 a.m. ET to discuss the fourth quarter and full year 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 WVE-N531 Clinical Trial
WVE-N531 is being evaluated in a Phase 1b/2a open-label study to evaluate the safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD), and clinical effects of intravenous (IV) WVE-N531 in patients with Duchenne muscular dystrophy (DMD). In the initial cohort of the trial, three 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. Based on positive initial results, Wave is initiating Part B (Phase 2) of the study to include up to ten boys with DMD, who will receive 10mg/kg of WVE-N531 administered biweekly. The primary objective will be measurement of dystrophin protein after 24 and 48 weeks of treatment. Additional objectives include PK, functional endpoints, as well as safety and tolerability.

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.

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. 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.

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 clinical trials, and the announcement of such events; the protocol, design and endpoints of our 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; 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 benefits of our therapeutic candidates compared to others; our ability to design compounds using multiple modalities and the anticipated benefits of that approach; the breadth and versatility of PRISM; the expected benefits of our stereopure oligonucleotides compared with stereorandom oligonucleotides; the potential benefits of our RNA editing capability, including our AIMers, compared to others; the status and progress of our 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 and the data that support our IP; the anticipated duration of our cash runway; our intended uses of capital; and our expectations regarding the impact of the COVID-19 pandemic and other global macro events beyond our control 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 our product candidates; actions of regulatory authorities 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; the effectiveness of our RNA editing 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 the indications we are pursuing; 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 and 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)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 88,497	$ 150,564
Prepaid expenses	7,932	6,584
Other current assets	2,108	5,416
Total current assets	98,537	162,564
Long-term assets:		
Property and equipment, net	17,284	22,266
Operating lease right-of-use assets	26,843	18,378
Restricted cash	3,660	3,651
Other assets	62	148
Total long-term assets	47,849	44,443
Total assets	$ 146,386	$ 207,007
Liabilities, Series A preferred shares and shareholders' equity (deficit)		

Current liabilities:		
Accounts payable	$ 16,915	$ 7,281
Accrued expenses and other current liabilities	17,552	14,861
Current portion of deferred revenue	31,558	37,098
Current portion of operating lease liability	5,496	4,961
Total current liabilities	71,521	64,201
Long-term liabilities:		
Deferred revenue, net of current portion	79,774	77,479
Operating lease liability, net of current portion	32,118	24,955
Other liabilities	190	—
Total long-term liabilities	112,082	102,434
Total liabilities	$ 183,603	$ 166,635
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2022 and 2021	$ 7,874	$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 86,924,643 and 59,841,116 shares issued and outstanding at December 31, 2022 and 2021, respectively	$ 802,833	$ 749,851
Additional paid-in capital	119,442	87,980
Accumulated other comprehensive income (loss)	(29)	181
Accumulated deficit	(967,337)	(805,514)
Total shareholders' equity (deficit)	(45,091)	32,498
Total liabilities, Series A preferred shares and shareholders' equity (deficit)	$ 146,386	$ 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 December 31,		Twelve Months Ended December 31,	
	2022	2021	2022	2021
Revenue	$ 1,239	$ 1,765	$ 3,649	$ 40,964
Operating expenses:				
Research and development	31,078	25,761	115,856	121,875
General and administrative	13,724	12,114	50,513	46,105
Total operating expenses	44,802	37,875	166,369	167,980
Loss from operations	(43,563)	(36,110)	(162,720)	(127,016)
Other income (expense), net:				
Dividend income and interest income, net	825	5	1,571	30
Other income (expense), net	(290)	1,116	7	4,537
Total other income (expense), net	535	1,121	1,578	4,567
Loss before income taxes	(43,028)	(34,989)	(161,142)	(122,449)
Income tax benefit (provision)	(681)	204	(681)	204
Net loss	$ (43,709)	$ (34,785)	$ (161,823)	$ (122,245)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.47)	$ (0.61)	$ (2.05)	$ (2.36)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	93,993,638	57,190,742	78,855,810	51,825,566
Other comprehensive income (loss):				
Net loss	$ (43,709)	$ (34,785)	$ (161,823)	$ (122,245)
Foreign currency translation	94	(77)	(210)	(208)
Comprehensive loss	$ (43,615)	$ (34,862)	$ (162,033)	$ (122,453)

Investor Contact:
Kate Rausch
617-949-4827
InvestorRelations@wavelifesci.com

Media Contact:
Alicia Suter

617-949-4817
asuter@wavelifesci.com

Source: Wave Life Sciences USA, Inc.