Wave Life Sciences Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Business Update

March 3, 2022

Clinical data from multiple novel, PN-modified stereopure oligonucleotides for ALS/FTD, DMD, and HD expected in 2022

GalNAc-AIMers restore therapeutically relevant levels of AAT for lung protection and reduce liver-damaging aggregates in preclinical study; IND enabling toxicology studies expected to initiate in 3Q 2022

FY2021 year-end cash total of $150.6 million providing runway into 2Q 2023

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

CAMBRIDGE, Mass., March 03, 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 fourth quarter and full year ended December 31, 2021 and provided a business update.

"Wave achieved multiple significant milestones in 2021, including successfully bringing PN chemistry into the clinic with the initiation of three new clinical trials with our next-generation RNA silencing and exon-skipping therapeutics, as well as demonstrating the first successful protein restoration with AIMers in preclinical *in vivo* models for the treatment of alpha-1 antitrypsin deficiency, also known as AATD. These accomplishments have positioned us to deliver several key datasets in 2022 to inform the potential of our novel oligonucleotides across tissues and modalities," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences.

"We continue to rapidly advance our AIMer RNA editing capabilities and are poised to deliver a first-in-class novel modality to address both lung and liver manifestations of AATD. We remain on track to select our first GalNAc-AIMer development candidate in the third quarter of this year, and we are leading the way with RNA base editing to address a wide array of genetic diseases, with potentially even more expansive applications through protein modulation. Lastly, our decade of investment in our PRISM platform has resulted in a robust and diverse pipeline, as well as internal GMP manufacturing capabilities that can be scaled to support our needs as well as potential new partners," continued Dr. Bolno.

Recent Business Highlights and Upcoming Milestones

Clinical silencing and exon skipping therapeutic programs:

Scientific publications:

- In February 2022, Wave announced two publications in the journal *Nucleic Acids Research (NAR)* supporting the incorporation of PN backbone chemistry modifications (PN chemistry) in stereopure oligonucleotides as a significant advancement for the therapeutic oligonucleotide field. In the multitude of *in vitro* and *in vivo* (animal) studies highlighted in Wave's papers, PN chemistry was shown to dramatically improve potency, distribution, and durability of effect. The papers explore the use of PN chemistry in stereopure silencing oligonucleotides (publication link) for central nervous system (CNS) diseases – designated as a Breakthrough Article by NAR -- and stereopure splicing oligonucleotides (publication link) for neuromuscular diseases.

WVE-N531 for Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping:

- WVE-N531 (PN-modified splicing oligonucleotide) is being evaluated in an open-label, intra-patient dose escalation clinical trial. Dose escalation is ongoing and being guided by tolerability and plasma PK, with possible cohort expansion informed by an assessment of drug distribution in muscle and biomarkers, including dystrophin, following multiple doses of WVE-N531.
- When comparing PN-modified compounds, including WVE-N531, to first-generation PS/PO (non-PN-modified) compounds, PN chemistry consistently leads to increased exon-skipping activity, increases in muscle exposure, longer half-life, and more durable effects in preclinical mouse and non-human primate studies. Based on an analysis of initial plasma PK from the starting single dose of WVE-N531 in Wave's ongoing clinical trial, there was a substantial increase in plasma concentrations and a clear increase in plasma half-life as compared to suvodirsen, Wave's first-generation PS/PO exon-skipping compound.

WVE-004 for C9orf72-associated amyotrophic lateral sclerosis (C9-ALS) and frontotemporal dementia (C9-FTD):

- FOCUS-C9 is an ongoing, double-blind, adaptive, Phase 1b/2a clinical trial of WVE-004. WVE-004 is an investigational stereopure PN-modified silencing oligonucleotide designed to selectively target transcript variants containing a

hexanucleotide repeat expansion (G_4C_2) associated with the *C9orf72* gene for the treatment of C9-ALS and C9-FTD.
- In January 2022, the Alzheimer's Drug Discovery Foundation (ADDF) and The Association for Frontotemporal Degeneration (AFTD) announced they had partnered to support Wave's FOCUS-C9 clinical trial, specifically the evaluation of fluid biomarkers, functional assessments, and digital biomarkers used in the study, potentially leading to clinically meaningful endpoints to inform drug development for FTD. The decision to support the FOCUS-C9 trial was made following a review by members of the Treat FTD Fund Joint Steering Committee of Wave's Phase 1b/2a study plan, preclinical data supporting the program and expertise of the study team.

WVE-003 targeting SNP3 for Huntington's disease (HD):

- SELECT-HD is an ongoing, double-blind, adaptive, Phase 1b/2a clinical trial of WVE-003. WVE-003 is an investigational stereopure PN-modified silencing oligonucleotide designed to selectively target the mutant allele of the *huntingtin* (mHTT) gene, while leaving the wild-type (healthy) HTT (wtHTT) protein relatively intact.
- In March 2022, Wave presented at the CHDI Foundation's 17 th Annual HD Therapeutics Conference, including a poster titled *"A novel quantitative wild-type huntingtin (wtHTT) protein biomarker method for human cerebrospinal fluid"* that highlights Wave's wtHTT assay, which is intended to assess preservation of wtHTT protein in CSF in the setting of mHTT targeting, including in the ongoing SELECT-HD clinical trial.

Upcoming clinical milestones:

- Wave expects to share clinical data in 2022 for WVE-004, WVE-003, and WVE-N531 to provide insight into the clinical effects of PN chemistry and enable decision-making for each program.

ADAR editing therapeutic programs (RNA editing using endogenous ADAR enzymes)

Scientific presentations:

- In January 2022, Wave gave an oral presentation titled "*Towards the development of a therapeutic RNA editing platform*" at the 3rd International Conference on Base Editing – Enzymes and Applications Deaminet 2022, which highlighted Wave's RNA editing platform, the ability of AIMers to restore expression of functional protein in preclinical models *in vivo* and modulate protein-protein interactions *in vitro*.
- Wave leadership will present at the upcoming 3rd RNA Editing Summit on April 5 – 7, 2022 in Boston.

AATD program updates and upcoming milestones:

- Wave today announced new preclinical data demonstrating restoration of functional AAT protein in a transgenic mouse model with GalNAc-conjugated SERPINA1 AIMers. At 19 weeks, AIMer treatment resulted in approximately 60% RNA editing of SERPINA1 transcript and circulating serum AAT levels (18.5 uM) in AIMer treated mice that were approximately 5-fold greater than PBS-treated controls.
- Today, Wave also shared a histological analysis that indicates reduction of liver aggregates in a transgenic mouse model at 19 weeks with AIMer treatment.
- In November 2021, Wave presented a poster at AASLD: The Liver Meeting, that included data demonstrating SERPINA1 AIMers achieve highly specific RNA editing *in vivo*, resulting in wild-type, M-AAT protein circulating in serum that was functional in a neutrophil elastase inhibition assay.
- Wave expects to select an AATD AIMer development candidate and initiate IND-enabling toxicology studies in the third quarter of 2022.

Fourth Quarter and Full Year 2021 Financial Results and Financial Guidance

Wave reported a net loss of $34.8 million in the fourth quarter of 2021, as compared to $28.8 million in the same period in 2020. Wave reported a net loss of $122.2 million for the year ended December 31, 2021, as compared to $149.9 million for the year ended December 31, 2020.

Revenue earned under the Takeda Collaboration in the fourth quarter of 2021 was $1.8 million, as compared to $9.4 million for the same period in 2020. The decrease in revenue year-over-year is mainly due to the amendment of Wave's collaboration with Takeda, which discontinued the Category 2 discovery research component of the Takeda Collaboration in exchange for an additional $22.5 million, which Wave received in October 2021 and accounted for in the third quarter of 2021. The Category 1 late-stage component of the Takeda Collaboration remains in effect and was unchanged by the amendment. During the year ended December 31, 2021, Wave earned $41.0 million under the Takeda Collaboration, as compared to $20.1 million earned under the Takeda Collaboration and the Pfizer Collaboration during the year ended December 31, 2020. The year-over-year increase is primarily driven by recognition of revenue related to the $22.5 million related to the Takeda Amendment.

Research and development expenses were $25.8 million in the fourth quarter of 2021 as compared to $30.0 million in the same period in 2020. Research and development expenses were $121.9 million in 2021, as compared to $130.9 million in 2020. The decrease in research and development expenses in the fourth quarter and full year was primarily due to decreased external expenses related to our previously disclosed discontinued PRECISION-HD programs, partially offset by increased internal and external expenses related to WVE-004, PRISM, including ADAR editing, and other ongoing programs.

General and administrative expenses were $12.1 million in the fourth quarter of 2021 as compared to $9.7 million in the same period in 2020. General

and administrative expenses were $46.1 million in 2021, as compared to $42.5 million in 2020. The increase in general and administrative expenses in the fourth quarter of 2021 and full year was driven by increases in compensation-related and other external general and administrative expenses.

As of December 31, 2021, Wave had $150.6 million in cash and cash equivalents as compared to $184.5 million as of December 31, 2020. The decrease in cash and cash equivalents was mainly due to Wave's year-to-date net loss of $122.2 million, partially offset by the receipt of $54.9 million in net proceeds under Wave's ATM equity program and funds of $52.5 million received from our collaboration with Takeda.

Wave expects that its existing cash and cash equivalents will enable the company to fund its operating and capital expenditure requirements into the second quarter 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 company's fourth quarter and full year 2021 financial results and provide a business update. The conference call may be accessed by dialing (866) 220-8068 (domestic) or (470) 495-9153 (international) and entering conference ID: 7694386. The live webcast may be accessed from the Investor Relations section of the Wave Life Sciences corporate website at ir.wavelifesciences.com. Following the webcast, a replay will be available on the website.

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 for decision-making and completion of our adaptive clinical trials, and the announcement of such events; the protocol, design and endpoints of our ongoing and planned 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 *in vitro* and *in vivo* 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 model; 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; 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, which may affect the initiation, timing and progress of clinical trials, including their receptiveness to our adaptive trial designs; our effectiveness in managing future clinical trials and regulatory interactions; 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; the continued development and acceptance of oligonucleotides as a class of medicines; 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)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		

Cash and cash equivalents	$ 150,564	$ 184,497
Current portion of accounts receivable	—	30,000
Prepaid expenses	6,584	10,434
Other current assets	5,416	5,111
Total current assets	162,564	230,042
Long-term assets:		
Property and equipment, net	22,266	29,198
Operating lease right-of-use assets	18,378	16,232
Restricted cash	3,651	3,651
Other assets	148	115
Total long-term assets	44,443	49,196
Total assets	$ 207,007	$ 279,238
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 7,281	$ 13,795
Accrued expenses and other current liabilities	14,861	11,971
Current portion of deferred revenue	37,098	91,560
Current portion of operating lease liability	4,961	3,714
Total current liabilities	64,201	121,040
Long-term liabilities:		
Deferred revenue, net of current portion	77,479	41,481
Operating lease liability, net of current portion	24,955	25,591
Other liabilities	—	474
Total long-term liabilities	102,434	67,546
Total liabilities	$ 166,635	$ 188,586
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2021 and 2020	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 59,841,116 and 48,778,678 shares issued and outstanding at December 31, 2021 and 2020, respectively	749,851	694,085
Additional paid-in capital	87,980	71,573
Accumulated other comprehensive income	181	389
Accumulated deficit	(805,514)	(683,269)
Total shareholders' equity	32,498	82,778
Total liabilities, Series A preferred shares and shareholders' equity	$ 207,007	$ 279,238

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,	
	2021	**2020**	**2021**	**2020**
Revenue	$ 1,765	$ 9,439	$ 40,964	$ 20,077
Operating expenses:				
Research and development	25,761	30,033	121,875	130,944
General and administrative	12,114	9,719	46,105	42,510
Total operating expenses	37,875	39,752	167,980	173,454
Loss from operations	(36,110)	(30,313)	(127,016)	(153,377)
Other income, net:				
Dividend income and interest income, net	5	24	30	568
Other income, net	1,116	659	4,537	2,058
Total other income, net	1,121	683	4,567	2,626
Loss before income taxes	(34,989)	(29,630)	(122,449)	(150,751)
Income tax benefit	204	841	204	841
Net loss	$ (34,785)	$ (28,789)	$ (122,245)	$ (149,910)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.61)	$ (0.59)	$ (2.36)	$ (3.82)

Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	57,190,742	48,777,001	51,825,566	39,227,618
Other comprehensive income (loss):				
Net loss	$ (34,785)	$ (28,789)	$ (122,245)	$ (149,910)
Foreign currency translation	(77)	88	(208)	122
Comprehensive loss	$ (34,862)	$ (28,701)	$ (122,453)	$ (149,788)

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