Wave Life Sciences Reports First Quarter 2021 Financial Results and Provides Business Update

May 13, 2021

Clinical trials underway with next-generation candidates incorporating PN chemistry

Clinical data from PN chemistry programs expected in 2022

In vivo ADAR editing data for AATD program on track for 1H 2021

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

CAMBRIDGE, Mass., May 13, 2021 (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 first quarter ended March 31, 2021 and provided a business update.

"Despite our PRECISION-HD results at the end of the first quarter, it has been a productive start of the year for Wave and our team remains focused on advancing our clinical trials for ALS/FTD, HD and DMD. These new trials mark the transition of our next-generation programs into the clinic. We expect clinical data that will provide insight into PN chemistry and enable decision making on next steps for these programs next year," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We have a deep and diverse pipeline of RNA therapeutics, each designed with our PN chemistry, which has been shown to increase potency, exposure and durability compared to our first-generation compounds in preclinical studies. We continue to produce compelling *in vivo* data, and we are advancing multiple programs for CNS indications, including Alzheimer's disease, Parkinson's disease and others, in collaboration with our partner Takeda. Our ADAR editing capability demonstrates the diversity of our genetic medicines toolkit and we are well-positioned to be leaders in the RNA editing field. We look forward to providing more updates on ADAR editing, including the first *in vivo* data from our AATD program, in the first half of this year."

Recent Business Highlights and Upcoming Milestones

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

- WVE-004 is an investigational antisense oligonucleotide designed to selectively target transcript variants containing a hexanucleotide repeat expansion (G_4C_2) in the C9orf72 gene, which is one of the most common genetic causes of the sporadic and inherited forms of ALS and FTD. WVE-004 uses novel PN backbone chemistry modifications.
- In February 2021, Wave published in *Nature Communications* the results of initial work to identify and validate its targeting strategy to achieve variant-selective knockdown of expansion-containing C9orf72 transcripts.
- In April 2021, during a platform presentation at the American Academy of Neurology (AAN) 2021 Virtual Annual Meeting, Wave highlighted preclinical *in vivo* data for WVE-004, which demonstrated potent and durable knockdown of more than 90% of polyGP dipeptide repeat (DPR) proteins in the spinal cord and at least 80% in the cortex, an effect that persisted for at least six months. C9orf72 protein was relatively unchanged over the same time period.
- This week, at the European Network to Cure ALS (ENCALS) meeting being held May 12 – May 14, Wave is presenting a poster introducing its FOCUS-C9 Phase 1b/2a trial design for WVE-004. The FOCUS-C9 trial is a global, multicenter, randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial to assess the safety and tolerability of intrathecal doses of WVE-004 for patients with C9-ALS and/or C9-FTD. Additional objectives include measurement of polyGP proteins in the cerebrospinal fluid (CSF), plasma and CSF pharmacokinetics, and exploratory biomarker and clinical endpoints. The FOCUS-C9 trial is designed to be adaptive and includes single- and multiple-ascending dose portions, with dose escalation and dosing frequency being guided by an independent safety committee.
- Wave has received regulatory and ethics approvals and site activation is underway for the FOCUS-C9 clinical trial, and Wave expects to initiate dosing in 2021.

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

- WVE-003 is Wave's next-generation HD candidate and Wave's first HD candidate that uses PN chemistry. WVE-003 is designed to selectively target the mutant allele of the *huntingtin* (mHTT) gene, while leaving the wild-type (wtHTT) protein relatively intact. Wave's approach to HD is guided by the recognition that, in addition to a gain of function of the mHTT protein, people with this disease have less wtHTT protein, leaving them with a smaller protective reservoir of healthy protein than unaffected individuals. A growing body of scientific evidence suggests that preserving as much of this essential protein as possible, when in the setting of stress from toxic mHTT protein, may be important for favorable clinical outcomes.
- In April 2021, at the 16th Annual CHDI Foundation Huntington's Disease Therapeutic Conference, Wave highlighted preclinical data for WVE-003, which showed selective reduction of mHTT mRNA *in vitro* and potent and durable knockdown of mHTT mRNA *in vivo.* Wave also introduced the design for the Phase 1b/2a clinical trial of WVE-003, called SELECT-HD. The multicenter, randomized, double-blind, placebo-controlled trial will assess the safety and tolerability of intrathecally administered WVE-003 for patients with early manifest Huntington's disease. Additional objectives include measurement of mHTT and wtHTT protein and exploratory pharmacokinetic, pharmacodynamic, clinical and MRI endpoints. The trial is designed to be adaptive, with dose escalation and dosing frequency being guided by an independent safety committee.
- Wave has received regulatory and ethics approvals and site activation is underway for the SELECT-HD clinical trial, and Wave expects to initiate dosing in 2021.

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

- WVE-N531 is Wave's first splicing candidate to incorporate PN chemistry, which Wave advanced following results of an *in vivo* study in double knock-out mice (dKO) that showed that an oligonucleotide designed with PN chemistry appeared to significantly increase dystrophin production and substantially improve survival, compared to oligonucleotides designed with Wave's first-generation chemistry.
- In March 2021, Wave initiated clinical development of WVE-N531 with the submission of a clinical trial application.

- Wave has received regulatory approval for a clinical trial of WVE-N531 to assess initial safety and dystrophin production in patients with DMD amenable to exon 53 skipping. Wave expects to initiate dosing in this trial in 2021.

ADAR editing:

- In March 2021, Wave presented a poster at the 2021 Keystone eSymposia on Precision Engineering of the Genome, Epigenome and Transcriptome highlighting the breadth of RNA editing data generated using its ADAR editing capability to date. This presentation illustrated editing activity across *in vivo* and *in vitro* systems, including *in vivo* editing in the CNS, using conjugated and non-conjugated oligonucleotides. Wave will also present these data in an oral presentation at the 24th American Society of Gene and Cell Therapy (ASGCT) Annual Meeting being held this week, May 11 – 14, 2021.
- Wave expects to present additional ADAR editing data at scientific congresses in 2021.

Alpha-1 antitrypsin deficiency (AATD) program with ADAR editing:

- Wave's AATD program, its first ADAR editing program, uses an oligonucleotide to correct the single RNA base mutation in mRNA coded by the *SERPINA1 Z* allele. ADAR editing may provide an ideal approach to treating AATD by increasing circulating levels of healthy alpha-1 antitrypsin (AAT) protein and reducing aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.
- To support the continued development of its AATD program, Wave has developed a proprietary humanized SERPINA1/ADAR model. Wave expects to share *in vivo* data from this model in the first half of 2021 and plans to submit these data for presentation at a scientific congress in 2021.

First Quarter 2021 Financial Results and Financial Guidance
Wave reported a net loss of $42.5 million in the first quarter of 2021 as compared to $47.5 million in the same period in 2020.

Research and development expenses were $33.4 million in the first quarter of 2021 as compared to $41.2 million in the same period in 2020. The year-over-year decrease was primarily due to the decrease in external expenses related to Wave's suvodirsen program, which was discontinued in December 2019, but had wind-down costs throughout 2020, as well as decreases in compensation-related expenses and other external expenses, partially offset by the increases in external expenses related to Wave's clinical and preclinical activities related to its HD programs and its *C9orf72* program for ALS and FTD.

General and administrative expenses were $10.1 million in the first quarter of 2021, as compared to $13.0 million in the same period in 2020. The year-over-year decrease was driven by decreases in compensation-related expenses and other external expenses.

Wave ended the first quarter of 2021 with $148.5 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, partially offset by the receipt of $8.0 million in net proceeds under Wave's at-the-market equity program. In April 2021, Wave received an additional $30.0 million in committed research support under its collaboration with Takeda.

Wave expects that its existing cash and cash equivalents, together with expected and committed cash from its existing collaboration, 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 first quarter and 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: 7430859. 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 commencement, patient enrollment, data readouts 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 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 anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; 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 compared to others; the benefit of nucleic acid therapeutics generally; the strength of our intellectual property; the anticipated duration of our cash runway; 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; our ability to maintain the company infrastructure and personnel needed to achieve our goals; the clinical results of our programs, 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; 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; the severity and duration of the COVID-19 pandemic 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)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 148,535	$ 184,497
Current portion of accounts receivable	30,000	30,000
Prepaid expenses	10,430	10,434
Other current assets	5,580	5,111
Total current assets	194,545	230,042
Long-term assets:		
Property and equipment, net	27,370	29,198
Operating lease right-of-use assets	15,720	16,232
Restricted cash	3,651	3,651
Other assets	1,361	115
Total long-term assets	48,102	49,196
Total assets	$ 242,647	$ 279,238
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 13,418	$ 13,795
Accrued expenses and other current liabilities	6,661	11,971
Current portion of deferred revenue	24,763	91,560
Current portion of operating lease liability	3,838	3,714
Total current liabilities	48,680	121,040
Long-term liabilities:		
Deferred revenue, net of current portion	108,278	41,481
Operating lease liability, net of current portion	24,587	25,591
Other liabilities	407	474
Total long-term liabilities	133,272	67,546
Total liabilities	$ 181,952	$ 188,586
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at March 31, 2021 and December 31, 2020	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 49,854,651 and 48,778,678 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	$ 702,649	$ 694,085
Additional paid-in capital	75,636	71,573
Accumulated other comprehensive income	269	389
Accumulated deficit	(725,733)	(683,269)
Total shareholders' equity	$ 52,821	$ 82,778
Total liabilities, Series A preferred shares and shareholders' equity	$ 242,647	$ 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 March 31,	
	2021	2020
Revenue	$ —	$ 4,161
Operating expenses:		
Research and development	33,393	41,158
General and administrative	10,078	12,996
Total operating expenses	43,471	54,154

Loss from operations	(43,471)	(49,993)
Other income, net:		
Dividend income and interest income, net	11	388
Other income, net	996	2,112
Total other income, net	1,007	2,500
Loss before income taxes	(42,464)	(47,493)
Income tax provision	—	—
Net loss	$ (42,464)	$ (47,493)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.86)	$ (1.38)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	49,101,606	34,461,505
Other comprehensive income (loss):		
Net loss	$ (42,464)	$ (47,493)
Foreign currency translation	(120)	6
Comprehensive loss	$ (42,584)	$ (47,487)

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