Wave Life Sciences Reports Fourth Quarter and Full Year 2019 Financial Results and Provides Business Update

March 2, 2020

Innovative pipeline of stereopure oligonucleotides focused on CNS diseases

32 mg data from both PRECISION-HD clinical trials on track for 2H 2020

Two additional CNS programs − SNP3 and C9orf72 − on track to initiate clinical development in 2H 2020

Wave to host investor conference call and webcast at 8:00 a.m. ET today

CAMBRIDGE, Mass., March 02, 2020 (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, 2019 and provided a business update.

"We continue to advance our innovative, CNS-focused pipeline of stereopure oligonucleotides across Huntington's disease, amyotrophic lateral sclerosis, frontotemporal dementia and other central nervous system diseases. Despite the disappointment of discontinuing our Duchenne program last year, we are advancing more than a dozen programs across discovery and development with several exciting milestones ahead in 2020," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "In December 2019, we shared the first clinical results from an allele-selective program for Huntington's disease. Initial results from PRECISION-HD2 demonstrated a reduction in mutant huntingtin protein, with a safety profile that supports the addition of a higher dose cohort, and no change in total huntingtin protein as compared to placebo. In the second half of 2020, we expect to initiate clinical development for our SNP3 program as well as our C9orf72 program, both of which have benefitted from novel advances in our PRISM platform. In addition, we are pleased by recent progress across multiple CNS programs we are working on in collaboration with Takeda. Finally, we presented proof-of-concept data for our RNA-editing program in January, which demonstrated endogenous ADAR engagement *in vitro*. We expect to have initial *in vivo* results in 2020, and we look forward to sharing further updates on this exciting new modality."

Business update
Wave is building a leading genetic medicines company focused on realizing the potential of stereopure oligonucleotides in diseases of the central nervous system, liver, and eye. Wave's pipeline includes more than a dozen programs across discovery and development, spans multiple modalities and targets, and is intended to deliver transformational medicines to patients and families.

Central nervous system (CNS) diseases

Updates for PRECISION-HD clinical trials of WVE-120101 and WVE-120102 in Huntington's disease

- *WVE-120101 and WVE-120102 allele-selectivity*: Investigational WVE-120101 and WVE-120102 are currently the only compounds in clinical development designed to selectively target the mutant allele of the huntingtin (mHTT) gene, while leaving the wild-type (wtHTT) relatively intact. The wtHTT protein is important for neuronal function, and there is increasing evidence that it may be neuroprotective in an adult brain. Additionally, Huntington's disease (HD) may be caused by a dominant gain of function in mHTT protein *and* a concurrent loss of function of wtHTT protein may be an important component of the pathophysiology of HD. Wave's allele-selective approach may also enable the company to address the pre-manifest, or asymptomatic, HD patient population in the future.
- *PRECISION-HD2*: In January 2020, Wave initiated dosing in a 32 milligram (mg) dose cohort in the PRECISION-HD2 Phase 1b/2a clinical trial of WVE-120102, a stereopure oligonucleotide designed to selectively target the mutant huntingtin (mHTT) mRNA transcript of SNP2 for HD. Wave is also assessing the potential for a next higher dose cohort to be added to the trial.
- Wave's ability to advance to higher dose cohorts was supported by initial PRECISION-HD2 clinical data, announced in December 2019, that demonstrated a statistically significant reduction of 12.4% in mHTT in cerebrospinal fluid (CSF) in an analysis comparing all patients treated with WVE-120102 to placebo. An analysis to assess a dose response across treatment groups (2, 4, 8 or 16 mg) suggested a statistically significant response in mHTT reduction at the highest doses tested (p=0.03). WVE-120102 was generally safe and well tolerated across all cohorts. There was no difference in total huntingtin protein compared to placebo.
- Data from the 32 mg dose cohort of the PRECISION-HD2 trial are expected in the second half of 2020.
- Enrollment continues in an open-label extension (OLE) study open to patients outside of the U.S. who participated in the Phase 1b/2a PRECISION-HD2 trial.
- *PRECISION-HD1*: The PRECISION-HD1 Phase 1b/2a clinical trial, Wave's clinical trial investigating WVE-120101, a stereopure oligonucleotide designed to selectively target the mHTT mRNA transcript of SNP1 for HD, is ongoing. Wave expects to initiate a 32 mg cohort to the PRECISION-HD1 trial and deliver topline clinical data from the PRECISION-HD1 trial, including a 32 mg dose cohort, in the second half of 2020.
- In February 2020, Wave initiated an OLE study open to patients outside of the U.S. who participated in the Phase 1b/2a PRECISION-HD1 trial.

Advancing third allele-selective Huntington's disease program (SNP3) towards clinical development .

- In February 2020, at the 15th annual CHDI Foundation Huntington's Disease Therapeutics Conference, Wave presented

preclinical data for its investigational SNP3 program. SNP3 represents ~40% of the HD population and, with overlap, up to 80% of the HD population carries at least one of SNP1, SNP2, and/or SNP3. In patient-derived neurons, Wave's allele-selective SNP3 compounds demonstrated more potent knockdown of mutant HTT in vitro than a pan-silencing active comparator. In addition, Wave's SNP3 compounds demonstrated potent and durable knockdown of mutant HTT in a transgenic mouse model for up to 12 weeks.
- Wave expects to initiate clinical development of its SNP3 program in the second half of 2020.

Advancing C9orf72 preclinical program for ALS and FTD towards clinical development

- Wave is advancing its C9orf72 preclinical program to potentially treat amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) and expects to initiate clinical development in the second half of 2020.Wave's C9orf72 program preferentially targets the transcript containing the hexanucleotide repeat expansion (G4C2) in the *C9orf72* gene.
- Wave's C9orf72 program led to substantial reduction of repeat containing *C9orf72* transcripts and dipeptides in both the spinal cord and cortex of a transgenic mouse model, while total C9orf72 protein was preserved.

Pipeline of CNS programs progressing in collaboration with Takeda

- The company is leveraging its learnings from PRISM ™to design additional stereopure oligonucleotides with optimized profiles for CNS indications, including Parkinson's, Alzheimer's and others as part of its ongoing collaboration with Takeda.

Ophthalmologic diseases

- In 2019, Wave's discovery efforts yielded two preclinical ophthalmology programs. The first program uses stereopure oligonucleotides to promote *USH2A* exon 13 skipping to address Usher Syndrome Type 2A. The second program uses stereopure oligonucleotides to selectively silence RhoP23H transcripts to address retinitis pigmentosa.

RNA-editing

- Wave is leveraging its proprietary PRISM platform to design novel RNA-editing therapeutics. Wave's technology uses endogenous ADAR (adenosine deaminases acting on RNA) enzymes via non-viral, free uptake of RNA editing oligonucleotides in a variety of primary human cell types *in vitro* with high efficiencies and has potential to be a best-in-class RNA editing modality.
- In January 2020, at the 1st International Conference on Base Editing – Enzymes and Applications (Deaminet 2020), Wave presented a poster titled "RNA Editing via Endogenous ADARs Using Stereopure Oligonucleotides." Wave observed preclinical editing efficiencies of up to 70% in primary hepatocytes and approximately 50% in bronchial epithelial cells without the need for viral or lipid nanoparticle (LNP) delivery vehicles. In addition, stereopure oligonucleotides achieved greater ADAR-mediated editing compared to stereorandom oligonucleotides across several distinct RNA transcripts in primary human hepatocytes, which validates that the technology is applicable across multiple sequences.
- Wave expects to share *in vivo* RNA editing data in 2020.

Neuromuscular disease

- In December 2019, Wave announced the discontinuation of suvodirsen development for patients with Duchenne muscular dystrophy (DMD). Wave plans to present additional findings from the Phase 1 open-label extension study of suvodirsen at the 2020 MDA Clinical and Scientific Conference in Orlando, Florida, which will take place from March 20 through March 25, 2020.

Fourth Quarter and Full Year 2019 Financial Results and Financial Guidance

Wave reported a net loss of $56.8 million in the fourth quarter of 2019 as compared to $37.9 million in the same period in 2018. The company reported a net loss of $193.6 million for the year ended December 31, 2019 as compared to $146.7 million for the year ended December 31, 2018. The increase in net loss in the fourth quarter and the year ended December 31, 2019 was largely driven by increased research and development efforts and continued organizational growth, both of which included costs and efforts, including manufacturing, in preparation for the potential commercialization of suvodirsen.

Research and development expenses were $49.1 million in the fourth quarter of 2019 as compared to $39.8 million in the same period in 2018. Research and development expenses for the full year were $175.4 million as compared to $134.4 million for the prior year. The increase in research and development expenses in the fourth quarter and full year was primarily due to increased external expenses related to our clinical activities, including our HD programs and our now discontinued DMD programs, as well as increased investments in PRISM and other research and development expenses.

General and administrative expenses were $13.8 million for the fourth quarter of 2019 as compared to $12.8 million for the same period in the prior year. General and administrative expenses were $48.9 million in 2019 as compared to $39.5 million in 2018. The increase in general and administrative expenses in the fourth quarter and full year was mainly driven by continued organizational growth to support Wave's 2019 corporate goals.

Wave ended 2019 with $147.2 million in cash and cash equivalents as compared to $174.8 million as of December 31, 2018. The decrease in cash and cash equivalents was primarily the result of Wave's year-to-date net loss of $193.6 million, partially offset by the $161.8 million in net proceeds from the January 2019 follow-on offering.

Wave expects that its existing cash and cash equivalents, together with expected and committed cash from existing collaborations, will enable Wave to fund its operating and capital expenditure requirements into the third quarter of 2021.

Investor Conference Call and Webcast

Wave management will host an investor conference call today at 8:00 a.m. ET to discuss the company's fourth quarter and full year 2019 operating

results and provide an update on the company's development programs. The conference call may be accessed by dialing (866) 220-8068 (domestic) or +1 (470) 495-9153 (international) and entering conference ID 3994836. The live webcast may be accessed by visiting the investor relations section of the Wave Life Sciences corporate website at www.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. 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 artificial intelligence-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 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 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 and our stereopure oligonucleotides compared with stereorandom oligonucleotides; the benefit of nucleic acid therapeutics generally; the strength of our intellectual property; and the anticipated duration of our cash runway. 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; our effectiveness in managing future clinical trials and regulatory interactions; the effectiveness of PRISM; 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; and competition from others developing therapies for similar indications, 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, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 147,161	$ 174,819
Current portion of accounts receivable	20,000	10,000
Prepaid expenses	9,626	6,587
Other current assets	8,689	10,867
Total current assets	185,476	202,273
Long-term assets:		
Accounts receivable, net of current portion	30,000	50,000
Property and equipment, net	36,368	39,931
Operating lease right-of-use assets	18,101	—
Restricted cash	3,647	3,625
Other assets	10,658	111
Total long-term assets	98,774	93,667
Total assets	$ 284,250	$ 295,940
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 9,073	$ 13,089
Accrued expenses and other current liabilities	16,185	14,736
Current portion of deferred rent	—	115
Current portion of deferred revenue	89,652	100,945

Current portion of lease incentive obligation	—	1,156
Current portion of operating lease liability	3,243	—
Total current liabilities	118,153	130,041
Long-term liabilities:		
Deferred rent, net of current portion	—	5,132
Deferred revenue, net of current portion	63,466	68,156
Lease incentive obligation, net of current portion	—	9,247
Operating lease liability, net of current portion	29,304	—
Other liabilities	1,721	2,142
Total long-term liabilities	94,491	84,677
Total liabilities	$ 212,644	$ 214,718
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2019 and 2018	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 34,340,690 and 29,472,197 shares issued and outstanding at December 31, 2019 and 2018, respectively	539,547	375,148
Additional paid-in capital	57,277	37,768
Accumulated other comprehensive income	267	153
Accumulated deficit	(533,359)	(339,721)
Total shareholders' equity	63,732	73,348
Total liabilities, Series A preferred shares and shareholders' equity	$ 284,250	$ 295,940

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,	
	2019	2018	2019	2018
Revenue	$ 2,400	$ 3,620	$ 15,983	$ 14,414
Operating expenses:				
Research and development	49,128	39,809	175,431	134,428
General and administrative	13,805	12,754	48,869	39,509
Total operating expenses	62,933	52,563	224,300	173,937
Loss from operations	(60,533)	(48,943)	(208,317)	(159,523)
Other income, net:				
Dividend income	736	1,014	4,912	3,368
Interest income, net	4	6	29	22
Other income (expense), net	3,023	9,933	9,738	9,549
Total other income, net	3,763	10,953	14,679	12,939
Loss before income taxes	(56,770)	(37,990)	(193,638)	(146,584)
Income tax provision	—	103	—	(69)
Net loss	$ (56,770)	$ (37,887)	$ (193,638)	$ (146,653)
Net loss per share attributable to ordinary shareholders —basic and diluted	$ (1.65)	$ (1.29)	$ (5.72)	$ (5.06)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	34,303,975	29,463,131	33,866,487	28,970,404
Other comprehensive income (loss):				
Net loss	$ (56,770)	$ (37,887)	$ (193,638)	$ (146,653)
Foreign currency translation	(15)	(28)	114	37
Comprehensive loss	$ (56,785)	$ (37,915)	$ (193,524)	$ (146,616)

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

Media Contact:
Alicia Suter
617-949-4817
asuter@wavelifesci.com

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