Wave Life Sciences Reports Fourth Quarter and Full Year 2020 Financial Results and Provides Business Update

March 4, 2021

Strong execution in 2020 sets stage for advancing five clinical programs and novel ADAR editing modality in 2021

Data from ongoing PRECISION-HD and OLE clinical trials for Huntington's disease on track for end of 1Q 2021

Moving towards first patient dosing in three clinical trials with pipeline candidates incorporating PN chemistry: WVE-003 (SNP3), WVE-004 (C9orf72) and WVE-N531 (Exon 53)

Cash runway expected into 2Q 2023

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

CAMBRIDGE, Mass., March 04, 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 fourth quarter and full year ended December 31, 2020 and provided a business update.

"Wave is entering 2021 with depth and diversity throughout our pipeline and platform, the result of focused and deliberate execution, and a steadfast commitment to leading a new era of RNA therapeutics. Despite headwinds from the COVID-19 pandemic, we advanced our pipeline, significantly evolved our platform, announced our first ADAR editing program and added considerable talent to our innovative and driven team," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We are poised to bring five clinical programs forward in 2021, including three programs in Huntington's disease, a fourth program for ALS and FTD and a fifth program for exon 53 skipping in DMD. We remain on track to announce data from the Phase 1b/2a PRECISION-HD1 and PRECISION-HD2 trials at the end of the first quarter of 2021 and are excited about adding our next set of clinical programs incorporating novel PN backbone chemistry modifications, which preclinically have been shown to increase potency, exposure and durability in our growing portfolio of investigational stereopure oligonucleotides. Finally, we strengthened our balance sheet in September 2020 to support our pipeline and discovery work, extending our cash runway into the second quarter of 2023 and ensuring Wave is well-positioned to unlock potential and growth well beyond 2021."

2020 Full Year and Recent Business Highlights and Upcoming Milestones

Three programs with novel PN backbone chemistry modifications expected to enter clinic in 2021:

- In August 2020, Wave introduced novel PN backbone chemistry modifications, an advancement from its PRISM™ discovery and drug development platform. In preclinical studies, these modifications have been shown to increase potency, exposure and durability across silencing, splicing and RNA editing modalities.
- Wave expects to initiate dosing in three clinical trials in 2021, which will assess target engagement, impact on key disease biomarkers, and initial safety of WVE-003 (targeting SNP3), WVE-004 (targeting C9orf72) and WVE-N531 (targeting exon 53).
- All three compounds were designed with PN backbone chemistry modifications, and insight from pharmacokinetic (PK) and pharmacodynamic (PD) studies using *in vivo* models, as well as learnings from Wave's first-generation programs.

Programs for Huntington's disease (HD): Wave is developing a unique portfolio of investigational stereopure oligonucleotides 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 lost one copy of the wtHTT allele, 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 is important for favorable health outcomes. Wave's allele-selective approach may also enable treatment in the premanifest setting, before onset of clinical disease.

PRECISION-HD and OLE clinical trials in HD (WVE-120101 and WVE-120102):

- The PRECISION-HD1 and PRECISION-HD2 Phase 1b/2a trials evaluating investigational WVE-120101 (SNP1) and WVE-120102 (SNP2), respectively, in patients with HD are ongoing. WVE-120101 and WVE-120102 are designed to selectively target the mHTT mRNA transcript that contains specific single nucleotide polymorphisms (SNPs).
- Open-label extension (OLE) clinical trials for patients outside of the U.S. who participated in the Phase 1b/2a PRECISION-HD trials are also ongoing.
- Wave expects to report biomarker and safety data from all cohorts of the PRECISION-HD2 trial, along with data from all completed cohorts up to and including the 16 mg cohort from the PRECISION-HD1 trial at the end of the first quarter of 2021. Wave also expects to report data from patients who have received multiple doses of 8 or 16 mg of WVE-120101 or WVE-120102 in the OLE trials at the end of the first quarter of 2021.

WVE-003 (SNP3) for HD:

- WVE-003 is Wave's first allele-selective HD candidate that uses PN backbone chemistry modifications and was developed using preclinical *in vivo* models to enable target engagement assessment of a specific single nucleotide polymorphism (SNP3). In preclinical studies, WVE-003 showed selective reduction of mHTT mRNA *in vitro,* and potent and durable knockdown of mHTT mRNA *in vivo*.

- In December 2020, Wave initiated clinical development of WVE-003 with the submission of a clinical trial application (CTA).
- Wave expects to initiate dosing in a Phase 1b/2a clinical trial of WVE-003 for patients with HD in 2021.

Publications:

- In December 2020, *in Molecular Therapy Methods & Clinical Development*, Wave published its haplotype phasing method using single-molecule real-time sequencing and a custom algorithm to determine bases at SNPs on mutant alleles. Accurate haplotype phasing of SNPs and the expanded CAG repeat of the *huntingtin* gene enables identification of patients with Huntington's disease eligible for allele-selective clinical studies.
- In May 2020, Wave's prospective observational study of the frequency of SNP1 and SNP2 in patients with HD was published in *Neurology Genetics*. The study confirms the feasibility of rapidly and prospectively identifying SNP1 and/or SNP2 in association with the mHTT allele in patients with HD, to enable allele-selective, personalized treatment approaches in eligible patients.

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

- In February 2021, Wave published in *Nature Communications* results of initial work to identify and validate its targeting strategy to achieve variant-selective knockdown of expansion-containing C9orf72 transcripts with stereopure oligonucleotides for the treatment of ALS and FTD. The results in the publication represent the foundational work that led to the development of Wave's clinical candidate, WVE-004, which uses PN backbone chemistry modifications.
- In December 2020, Wave initiated clinical development of WVE-004 with the submission of a CTA.
- In August 2020, Wave presented preclinical *in vivo* data for WVE-004, which demonstrated potent and durable knockdown of more than 90% of poly GP dipeptide repeat (DPR) protein in the spinal cord and at least 80% in the cortex, an effect that persisted for at least six months. Healthy C9orf72 protein was relatively unchanged over the same time period.
- Wave expects to initiate dosing in a Phase 1b/2a clinical trial of WVE-004 for both patients with C9-ALS and patients with C9-FTD 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 backbone chemistry modifications.
- In a recently completed *in vivo* study of double knock-out mice (a model lacking dystrophin and utrophin protein with a severe phenotype), an oligonucleotide designed with PN backbone chemistry modifications appeared to significantly increase dystrophin production and substantially improve survival.
- In a planned clinical trial, Wave will assess dystrophin production and initial safety in patients with DMD amenable to exon 53 skipping.
- Wave expects to submit a CTA for WVE-N531 by the end of the first quarter of 2021.

Central nervous system (CNS) programs in collaboration with Takeda:

- Wave is utilizing PN backbone chemistry modifications to design stereopure oligonucleotides for CNS indications, including Alzheimer's disease, Parkinson's disease and others, as part of its ongoing collaboration with Takeda. Wave continues to produce compelling *in vivo* data and progress multiple discovery programs towards portfolio entry and candidate nomination.
- In the fourth quarter of 2020, Wave achieved the first demonstration of widespread target engagement in the CNS of non-human primates (NHPs) for the most advanced therapeutic program in the collaboration. Approximately 90% knockdown of the target mRNA was observed one month after a single 12 mg intrathecal dose, and the therapeutic candidate distributed widely across relevant CNS tissues.

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

- Wave's AATD program, its first ADAR editing program, will target the G-to-A disease-causing mutation in mRNA coded by the *SERPINA1* Z allele. By correcting the single RNA base mutation, ADAR editing may provide an ideal approach for increasing circulating levels of wild-type alpha-1 antitrypsin (AAT) protein and reducing aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.
- In November 2020, Wave presented *in vitro* data in a primary hepatocyte *SERPINA1* Z allele cell model, which demonstrated that editing the Z transcript back to wild-type prevents protein misfolding and increases secretion of edited AAT protein from hepatocytes.
- Wave expects to deliver in *vivo* data supporting the continued development of its AATD program in the first half of 2021.

ADAR editing platform modality:

- Wave's novel RNA editing modality incorporates PN backbone chemistry modifications and uses endogenous ADAR (adenosine deaminases acting on RNA) enzymes via free uptake (non-viral, no nanoparticles) of A-to-I (G) RNA editing oligonucleotides. ADAR editing has the potential to unlock many new therapeutic applications, including restoration, modification or upregulation of proteins.

Fourth Quarter and Full Year 2020 Financial Results and Financial Guidance

Wave reported a net loss of $28.8 million in the fourth quarter of 2020 as compared to $56.8 million in the same period in 2019. The company reported a net loss of $149.9 million for the year ended December 31, 2020 as compared to $193.6 million for the year ended December 31, 2019.

Research and development expenses were $30.0 million in the fourth quarter of 2020 as compared to $49.1 million in the same period in 2019. Research and development expenses were $130.9 million in 2020, as compared to $175.4 million in 2019. The decrease in research and development expenses in the fourth quarter and full year was primarily due to the decrease in external expenses related to Wave's decision to discontinue its suvodirsen program in December 2019, as well as decreases in compensation-related expenses and other external expenses driven by Wave's February 2020 cost reduction plan, 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 $9.7 million in the fourth quarter of 2020, as compared to $13.8 million in the same period in 2019. General and administrative expenses were $42.5 million in 2020, as compared to $48.9 million in 2019. The decrease in general and administrative expenses in the fourth quarter and full year was primarily driven by the February 2020 cost reduction plan, which led to decreases in compensation-related expenses and other external expenses.

Wave ended 2020 with $184.5 million in cash and cash equivalents as compared to $147.2 million as of December 31, 2019. During 2020, Wave substantially extended its cash runway, largely by raising $93.7 million in net proceeds from its September 2020 public offering and $59.9 million in net proceeds from its at-the-market equity program.

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 8:00 a.m. ET to discuss the company's fourth quarter and full year 2020 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: 6269069. 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 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; 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)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 184,497	$ 147,161
Current portion of accounts receivable	30,000	20,000
Prepaid expenses	10,434	9,626

Other current assets	5,111	8,689
Total current assets	230,042	185,476
Long-term assets:		
Accounts receivable, net of current portion	—	30,000
Property and equipment, net	29,198	36,368
Operating lease right-of-use assets	16,232	18,101
Restricted cash	3,651	3,647
Other assets	115	10,658
Total long-term assets	49,196	98,774
Total assets	$ 279,238	$ 284,250
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 13,795	$ 9,073
Accrued expenses and other current liabilities	11,971	16,185
Current portion of deferred revenue	91,560	89,652
Current portion of operating lease liability	3,714	3,243
Total current liabilities	121,040	118,153
Long-term liabilities:		
Deferred revenue, net of current portion	41,481	63,466
Operating lease liability, net of current portion	25,591	29,304
Other liabilities	474	1,721
Total long-term liabilities	67,546	94,491
Total liabilities	$ 188,586	$ 212,644
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2020 and 2019	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 48,778,678 and 34,340,690 shares issued and outstanding at December 31, 2020 and 2019, respectively	694,085	539,547
Additional paid-in capital	71,573	57,277
Accumulated other comprehensive income	389	267
Accumulated deficit	(683,269)	(533,359)
Total shareholders' equity	82,778	63,732
Total liabilities, Series A preferred shares and shareholders' equity	$ 279,238	$ 284,250

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,	
	2020	2019	2020	2019
Revenue	$ 9,439	$ 2,400	$ 20,077	$ 15,983
Operating expenses:				
Research and development	30,033	49,128	130,944	175,431
General and administrative	9,719	13,805	42,510	48,869
Total operating expenses	39,752	62,933	173,454	224,300
Loss from operations	(30,313)	(60,533)	(153,377)	(208,317)
Other income, net:				
Dividend income	24	736	584	4,912
Interest income (expense), net	—	4	(16)	29
Other income, net	659	3,023	2,058	9,738
Total other income, net	683	3,763	2,626	14,679
Loss before income taxes	(29,630)	(56,770)	(150,751)	(193,638)
Income tax benefit (provision), net	841	—	841	—
Net loss	$ (28,789)	$ (56,770)	$ (149,910)	$ (193,638)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.59)	$ (1.65)	$ (3.82)	$ (5.72)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	48,777,001	34,303,975	39,227,618	33,866,487
Other comprehensive income (loss):				
Net loss	$ (28,789)	$ (56,770)	$ (149,910)	$ (193,638)
Foreign currency translation	88	(15)	122	114
Comprehensive loss	$ (28,701)	$ (56,785)	$ (149,788)	$ (193,524)

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