



Wave Life Sciences Reports Third Quarter 2020 Financial Results and Provides Business Update

November 9, 2020

Results from all cohorts of PRECISION-HD1 and PRECISION-HD2 clinical trials and initial OLE data on track for 1Q 2021

Dosing in three new clinical trials with novel compounds incorporating PN chemistry and targeting SNP3 in HD, C9orf72 in ALS / FTD and exon 53 skipping in DMD expected in 2021

Alpha-1 antitrypsin deficiency announced as first ADAR editing program, with potential to address both lung and liver manifestations of the disease through correction of single RNA base mutation

Strengthened balance sheet with equity financing; cash runway extended into 2Q 2023

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

CAMBRIDGE, Mass., Nov. 09, 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 third quarter ended September 30, 2020 and provided a business update.

"The substantial progress made by Wave's research and clinical teams during the third quarter has ushered in a new phase for the company, during which we are rapidly advancing several new programs incorporating our novel PN backbone chemistry modification. We are on track to file clinical trial applications for WVE-003 for Huntington's disease and WVE-004 for amyotrophic lateral sclerosis and frontotemporal dementia this quarter. In addition, we are announcing today our plan to submit a clinical trial application in the first quarter of 2021 for a third PN backbone-containing molecule, WVE-N531 for patients with Duchenne muscular dystrophy who have mutations amenable to exon 53 skipping," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "We are also excited to announce our first ADAR editing target, the *SERPINA1* gene transcript, where a single base mutation is often the cause of alpha-1 antitrypsin deficiency. Using our unique ADAR editing capability to correct the RNA transcript, we will have the opportunity to address both liver and lung manifestations of the disease."

"The 32 mg cohorts in the PRECISION-HD1 and PRECISION-HD2 Phase 1b/2a clinical trials continue to move ahead, and we look forward to sharing results from all cohorts, as well as initial data from the ongoing open-label extension trials, in the first quarter of 2021. We are well-positioned to progress our planned and existing programs with our current cash balance."

Recent Business Highlights

PRECISION-HD 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 over a lifetime with the disease.

PRECISION-HD and OLE trials of WVE-120101 and WVE-120102:

- The PRECISION-HD1 and PRECISION-HD2 Phase 1b/2a clinical trials evaluating investigational WVE-120101 and WVE-120102, stereopure oligonucleotides designed to selectively target the mHTT mRNA transcript that contains SNP rs362307 (SNP1) and rs362331 (SNP2), respectively, in patients with HD are ongoing.
- 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.
- In the first quarter of 2021, Wave expects to report data from all cohorts in both PRECISION-HD trials, including the 32 mg dose cohorts, as well as data from patients who received multiple doses of 8 or 16 mg of WVE-120101 or WVE-120102 in the OLE trials.

HD SNP3 program (WVE-003):

- Wave is developing a third allele-selective HD candidate, WVE-003, which is designed to selectively target an undisclosed SNP on the mHTT mRNA transcript (SNP3), while leaving wtHTT protein relatively intact. Between its SNP1, SNP2 and SNP3-targeted molecules, Wave has the potential to provide allele-selective options for up to 80% of people with HD.
- In preclinical studies, WVE-003 showed selective reduction of mHTT mRNA *in vitro*, and potent and durable knockdown of mHTT mRNA *in vivo*.
- WVE-003 incorporates Wave's novel PN chemistry into its design.
- Wave expects to initiate clinical development of WVE-003 with the submission of a clinical trial application (CTA) in the fourth quarter of 2020.

C9orf72 program (WVE-004) for amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD): WVE-004 is designed to selectively target the transcript variants containing the hexanucleotide repeat expansion (G4C2) in the *C9orf72* gene. G4C2 expansions in the *C9orf72* gene lead to reduced expression of healthy protein, accumulation of repeat-containing transcripts and RNA binding proteins into nuclear RNA foci, and aberrant expression of neurotoxic dipeptide repeat proteins (DPRs).

- In preclinical studies in transgenic mice following two intracerebroventricular administered doses, WVE-004 showed potent

and durable knockdown of repeat-containing transcripts and DPRs while sparing healthy C9orf72 protein over a period of six months.

- WVE-004 incorporates Wave's novel PN chemistry into its design.
- Wave expects to initiate clinical development of WVE-004 with the submission of a CTA in the fourth quarter of 2020.

Exon 53 program (WVE-N531) for Duchenne muscular dystrophy (DMD): Based on compelling *in vitro* and *in vivo* preclinical results from compounds incorporating Wave's novel PN chemistry, Wave is advancing WVE-N531 to explore splicing in dystrophic muscle. Planning is underway for a clinical trial to assess dystrophin production and initial safety in patients with DMD amenable to exon 53 skipping.

- WVE-N531 induced a dose-dependent increase in dystrophin production (up to 71%) *in vitro* in DMD patient-derived myoblasts.
- In an ongoing *in vivo* study of double knock-out mice (a model lacking dystrophin and utrophin protein with a severe phenotype), an oligonucleotide with PN backbone chemistry modifications appeared to significantly increase dystrophin production and substantially improve muscle function and survival.
- WVE-N531 incorporates Wave's novel PN chemistry into its design.
- Wave expects to submit a CTA for WVE-N531 in the first quarter of 2021.

SERPINA1 program for alpha-1 antitrypsin deficiency (AATD) with ADAR-mediated RNA editing (ADAR editing): Wave announced today that it is applying its ADAR editing platform capability to develop a potential novel treatment for AATD aimed at addressing the lung and liver manifestations of the disease.

- AATD is a rare, inherited genetic disorder that is commonly caused by a single G-to-A point mutation in the *SERPINA1* gene, called the *SERPINA1* Z allele. This mutation leads to misfolding and aggregation of alpha-1 antitrypsin (AAT) protein in hepatocytes and a lack of functional AAT in the lungs. People with AATD typically exhibit progressive lung damage, liver damage or both, leading to frequent hospitalizations and potentially terminal lung disease and/or liver disease. The few approved therapies for AATD modestly increase circulating levels of AAT in those with the lung pathology; there are no approved therapies to address the liver pathology. Approximately 250,000 people worldwide are homozygous for the Z allele, which is the most severe form of the disease.
- Wave's novel RNA editing platform capability uses endogenous ADAR (adenosine deaminases acting on RNA) enzymes via free uptake (non-viral, no nanoparticles) of A-to-I (G) RNA editing oligonucleotides, making this a potentially best-in-class modality for correcting 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 AAT protein and reducing aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.
- In a primary hepatocyte *SERPINA1* Z cell model, editing the Z transcript back to wild-type prevented protein misfolding and increased secretion from hepatocytes.
- Wave is developing a proprietary *in vivo* model system, which uses human ADAR and human target transcript, to support the ongoing development of its ADAR editing platform. Data from its humanized *SERPINA1*/ADAR model are expected in the first half of 2021.
- Wave's *SERPINA1* program and ADAR editing platform capability incorporate the company's novel PN chemistry.

Central nervous system (CNS) programs in collaboration with Takeda: Wave is leveraging learnings from PRISM™, the company's proprietary discovery and drug development platform, to design additional stereopure oligonucleotides with optimized profiles for CNS indications, including in Alzheimer's disease, Parkinson's disease and others, as part of its ongoing collaboration with Takeda.

- Wave is utilizing PN backbone chemistry modifications to produce compelling *in vivo* data and actively progress up to six preclinical targets.
- In an *in vivo* study in 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. The therapeutic candidate distributed widely across multiple relevant CNS tissues.

Novel PN chemistry announced at Analyst & Investor Research Webcast: On August 25, 2020, Wave held an Analyst and Investor Research Webcast to highlight recent advancements to PRISM, including the expansion of its repertoire of backbone modifications with the introduction of PN backbone chemistry.

- PN chemistry is a backbone modification that involves replacing a non-bridging Oxygen atom with a Nitrogen-containing moiety.
- In preclinical experiments, judicious use of PN backbone chemistry modifications in stereopure oligonucleotides have generally increased potency, exposure and durability across Wave's silencing, splicing and editing modalities.
- Wave's current preclinical and discovery-stage programs incorporate PN backbone chemistry modifications.

Third Quarter 2020 Financial Results and Financial Guidance

As of September 30, 2020, Wave had \$216.4 million in cash and cash equivalents as compared to \$147.2 million as of December 31, 2019. During the third quarter of 2020, Wave substantially extended its cash runway by raising \$93.7 million in net proceeds from its September 2020 public offering and \$48 million in net proceeds from its at-the-market equity program, and receiving \$16.8 million in refundable tax credits.

Wave reported a net loss of \$33.1 million in the third quarter of 2020 as compared to \$50.7 million in the same period in 2019.

Research and development expenses were \$28.3 million in the third quarter of 2020 as compared to \$44.6 million in the same period in 2019. The decrease in research and development expenses in the third quarter was primarily due to decreased external expenses related to suvodirsen, due to Wave's December 2019 decision to discontinue the program, as well as decreased headcount and other external expenses driven by Wave's February 2020 cost reduction plan, partially offset by increased 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 \$9.6 million in the third quarter of 2020 as compared to \$12.5 million in the same period in 2019. The decrease in general and administrative expenses in the third quarter of 2020 was primarily due to the February 2020 cost reduction plan, which included a workforce reduction.

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 third quarter 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: 3563968. 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.

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; 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 severity and duration of the COVID-19 pandemic and its potentially negative impact on the conduct of, and the timing of enrollment, completion and reporting with respect to, our clinical trials; any other impacts on our business as a result of or related to the COVID-19 pandemic; 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 PN backbone chemistry; 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; 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)

	<u>September 30, 2020</u>	<u>December 31, 2019</u>
Assets		
Current assets:		
Cash and cash equivalents	\$ 216,363	\$ 147,161
Current portion of accounts receivable	30,000	20,000
Prepaid expenses	7,966	9,626
Other current assets	4,101	8,689
Total current assets	<u>258,430</u>	<u>185,476</u>
Long-term assets:		
Accounts receivable, net of current portion	—	30,000
Property and equipment, net	31,116	36,368
Operating lease right-of-use assets	16,725	18,101

Restricted cash	3,650	3,647
Other assets	140	10,658
Total long-term assets	51,631	98,774
Total assets	<u>\$ 310,061</u>	<u>\$ 284,250</u>
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	\$ 9,699	\$ 9,073
Accrued expenses and other current liabilities	10,182	16,185
Current portion of deferred revenue	86,192	89,652
Current portion of operating lease liability	3,591	3,243
Total current liabilities	<u>109,664</u>	<u>118,153</u>
Long-term liabilities:		
Deferred revenue, net of current portion	56,288	63,466
Operating lease liability, net of current portion	26,574	29,304
Other liabilities	1,420	1,721
Total long-term liabilities	<u>\$ 84,282</u>	<u>\$ 94,491</u>
Total liabilities	<u>\$ 193,946</u>	<u>\$ 212,644</u>
Series A preferred shares, par value; shares issued and outstanding at September 30, 2020 and December 31, 2019	<u>\$ 7,874</u>	<u>\$ 7,874</u>
Shareholders' equity:		
Ordinary shares, par value; 48,769,049 and 34,340,690 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	\$ 694,066	\$ 539,547
Additional paid-in capital	68,354	57,277
Accumulated other comprehensive income	301	267
Accumulated deficit	(654,480)	(533,359)
Total shareholders' equity	<u>\$ 108,241</u>	<u>\$ 63,732</u>
Total liabilities, Series A preferred shares and shareholders' equity	<u>\$ 310,061</u>	<u>\$ 284,250</u>

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2020	2019	2020	2019
Revenue	\$ 3,450	\$ 2,929	\$ 10,638	\$ 13,583
Operating expenses:				
Research and development	28,275	44,585	100,911	126,303
General and administrative	9,590	12,523	32,791	35,064
Total operating expenses	<u>37,865</u>	<u>57,108</u>	<u>133,702</u>	<u>161,367</u>
Loss from operations	(34,415)	(54,179)	(123,064)	(147,784)
Other income (expense), net:				
Dividend income	40	1,208	560	4,176
Interest income (expense), net	(17)	6	(16)	25
Other income, net	1,292	2,239	1,399	6,715
Total other income, net	<u>1,315</u>	<u>3,453</u>	<u>1,943</u>	<u>10,916</u>
Loss before income taxes	(33,100)	(50,726)	(121,121)	(136,868)
Income tax provision	—	—	—	—
Net loss	<u>\$ (33,100)</u>	<u>\$ (50,726)</u>	<u>\$ (121,121)</u>	<u>\$ (136,868)</u>
Net loss per share attributable to ordinary shareholders—basic and diluted	<u>\$ (0.86)</u>	<u>\$ (1.48)</u>	<u>\$ (3.36)</u>	<u>\$ (4.06)</u>
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	<u>38,364,224</u>	<u>34,281,203</u>	<u>36,021,256</u>	<u>33,719,055</u>
Other comprehensive income (loss):				
Net loss	\$ (33,100)	\$ (50,726)	\$ (121,121)	\$ (136,868)

Foreign currency translation
Comprehensive loss

	23	2	34	129
	<u>\$ (33,077)</u>	<u>\$ (50,724)</u>	<u>\$ (121,087)</u>	<u>\$ (136,739)</u>

Investor Contact:

Kate Rausch
617-949-4827
krausch@wavelifesci.com

Graham Morrell
781-686-9600
gmorrell@wavelifesci.com

Media Contact:

Alicia Suter
617-949-4817
asuter@wavelifesci.com



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