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

November 10, 2021

Strengthened balance sheet with approximately $52 million; focusing additional investment in RNA editing programs led by hepatic editing

Optimized AIMers for AATD program demonstrate potent, highly specific RNA editing and restoration of functional AAT protein substantially above therapeutic threshold; potential for best-in-class, potent and durable RNA editing in vivo in multiple preclinical models and tissues

Dosing ongoing in three clinical programs (WVE-004, WVE-003, WVE-N531); data being generated through 2022 to enable decision-making

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

CAMBRIDGE, Mass., Nov. 10, 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 third quarter ended September 30, 2021 and provided a business update.

“In the third quarter, we achieved several important milestones including providing a comprehensive update on our potentially best-in-class ADAR editing capability and the initiation of dosing in three clinical trials evaluating our next-generation stereopure PN-modified oligonucleotides,” said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. “RNA editing is a novel therapeutic modality that greatly expands our landscape of addressable genetically defined diseases. We are leading the way in this new field and quickly working toward announcing our first ADAR editing development candidate for our alpha-1 antitrypsin deficiency program next year. With this program, we are on a path to generate proof of principle that we can harness human biological machinery to edit RNA for the treatment of genetic diseases of the liver, CNS, and beyond.”

“Our robust and diversified pipeline is driven by our PRISM platform, which enables a unique ability to design and optimize oligonucleotides with novel, stereopure backbone modifications, including PN chemistry. We expect data being generated from our three ongoing clinical trials will enable us to make decisions on next steps for the programs next year. Finally, we recently strengthened our balance sheet via our at-the-market facility and funds received from Takeda under the terms of the amendment, leaving us well-capitalized to deliver on our portfolio, including advancing our first ADAR editing program toward the clinic and expanding our AIMer pipeline to include additional indications.”

ADAR editing capability recent events and upcoming milestones

Leading RNA editing capability using AIMers to harness endogenous ADAR enzymes

- Wave’s RNA editing capability leverages widely expressed endogenous ADAR enzymes to achieve highly specific A-to-I (G) RNA editing using stereopure oligonucleotides, called “AIMers,” with and without GalNAc conjugation, to edit RNA in the liver, central nervous system (CNS), and other tissues.
- In September 2021, during its Analyst and Investor Research Webcast, Wave presented new preclinical data that demonstrated potent and durable editing of UGP2 mRNA out to at least four months post-dose in multiple regions of mouse CNS. Wave is applying ADAR editing to multiple therapeutic targets in the CNS, including restoring functional MECP2 protein for the treatment of Rett Syndrome.
- Wave also presented preclinical data demonstrating up to 50% editing of UGP2 mRNA in the posterior of the eye of mice at one-month post-single intravitreal injection and ACTB RNA editing in non-human primates (NHPs) using systemic administration, including in the kidneys, liver, lungs, and heart, as well as editing of ACTB in multiple immune cell types *in vitro*.
- Wave expects to share additional ADAR editing data using AIMers in scientific publications and presentations in 2022.

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

- Wave’s AATD program, its first therapeutic ADAR editing program, uses stereopure oligonucleotides to correct the single base mutation in mRNA coded by the *SERPINA1 Z* allele. Restoring circulating levels of healthy alpha-1 antitrypsin (M-AAT) protein and reducing aggregation in the liver of mutant protein (Z-AAT) with RNA editing could potentially address both the lung and liver manifestations of the disease simultaneously.
- In September 2021, during its Analyst and Investor Research Webcast, Wave shared new *in vivo* data demonstrating durable restoration of M-AAT protein in the liver of transgenic mice with human SERPINA1 and human ADAR following initial doses of a GalNAc-conjugated SERPINA1 AIMer. Using PRISM chemistry optimization, Wave AIMers can achieve highly specific editing of up to 50% of SERPINA1 mRNA *in vivo* and restore AAT protein in serum to a level four-fold higher than phosphate-buffered saline (PBS) control (or more than 15 micromolar).
- Ongoing and planned preclinical studies are assessing durability, dose response, pharmacokinetics, and pharmacodynamics. Wave also plans to assess reduction of Z-AAT aggregates in the liver and changes in liver pathology in its transgenic mouse model, with data expected in 2022.

- Wave expects to announce its AATD AIMer development candidate in 2022.

Clinical silencing and exon skipping programs and upcoming milestones

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

- WVE-004 is an investigational stereopure antisense oligonucleotide designed to selectively target transcript variants containing a hexanucleotide repeat expansion (G_4C_2) associated with 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 Wave's novel PN backbone chemistry modifications (PN chemistry).
- In July 2021, Wave announced the initiation of dosing in the Phase 1b/2a FOCUS-C9 clinical trial, which is adaptive, with an independent committee to guide dose level and dosing frequency.

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

- WVE-003, Wave's first HD candidate to use PN chemistry and leverage transgenic models to assess target engagement *in vivo,* is designed to selectively target the mutant allele of the *huntingtin* (mHTT) gene, while leaving the wild-type (healthy) HTT (wtHTT) protein relatively intact. Wave's approach to HD is guided by the recognition that people with HD have less wtHTT protein compared to unaffected individuals and 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 September 2021, Wave announced the initiation of dosing in the Phase 1b/2a SELECT-HD clinical trial of WVE-003 in patients with early manifest HD. The SELECT-HD trial is adaptive, with an independent committee to guide dose level and dosing frequency.

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

- WVE-N531 is Wave's first stereopure splicing candidate and first systemically administered candidate to incorporate PN chemistry.
- In September 2021, Wave announced the initiation of dosing in an open-label clinical trial of WVE-N531 dosed intravenously bi-weekly in patients with DMD amenable to exon 53 skipping. Dose level and dosing frequency will be guided by tolerability and plasma PK, with possible cohort expansion driven by an assessment of drug distribution in muscle and biomarkers, including dystrophin.

Upcoming clinical milestones:

- Wave expects to generate clinical data through 2022 from WVE-004, WVE-003, and WVE-N531 to provide insight into the clinical effects of PN chemistry and enable decision-making regarding next steps for each program.

Corporate developments

- In October 2021, Wave issued and sold an aggregate block of approximately $30 million in ordinary shares through its at-the-market (ATM) equity program, based on interest received from new and existing shareholders following its Analyst and Investor Research Webcast in September 2021. Wave intends to use the additional capital to accelerate its RNA editing capability, led by its AATD program.
- In October 2021, Wave announced an amendment to its ongoing collaboration with Takeda, which streamlined the collaboration and allows Wave to advance or partner early-stage CNS programs, including those using ADAR editing. Wave received $22.5 million from Takeda under the terms of the amendment. The amendment did not impact the late-stage component of the collaboration, including Takeda's option to co-develop and co-commercialize WVE-004 and WVE-003. Should Takeda opt in on any of these programs, Wave would receive an opt-in payment, global costs and potential profits would be shared 50:50, and Wave would be eligible to receive development and commercial milestone payments.

Third quarter 2021 financial results and financial guidance

Wave reported a net loss of $6.2 million in the third quarter of 2021 as compared to $33.1 million in the same period in 2020.

Revenue earned during the three months ended September 30, 2021 was $36.4 million, as compared to $3.4 million for the three months ended September 30, 2020. The increase in revenue year-over-year is primarily driven by the $22.5 million paid as part of the amendment to Wave's collaboration agreement with Takeda, which was recognized as revenue in the three months ended September 30, 2021, as well as the recognition of the remaining revenue related to Category 2 research support payments previously paid by Takeda.

Research and development expenses were $31.1 million in the third quarter of 2021 as compared to $28.3 million in the same period in 2020. The increase in research and development expenses in the third quarter was primarily due to increased external expenses related to preclinical programs and compensation-related expenses, partially offset by decreased external expenses related to our discontinued programs.

General and administrative expenses were $12.9 million in the third quarter of 2021 as compared to $9.6 million in the same period in 2020. The

increase in general and administrative expenses in the third quarter of 2021 was driven by increases in compensation-related and other external general and administrative expenses.

As of September 30, 2021, Wave had $123.9 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 $87.5 million, partially offset by the receipt of $21.2 million in proceeds under Wave's ATM equity program through September 30, 2021.

Subsequently, in October 2021 Wave received an additional $52.1 million in cash, including $22.5 million from Takeda under the terms of the amendment to Wave's collaboration agreement with Takeda, and $29.6 million in proceeds under its ATM equity program from a block sale of ordinary shares based on interest received from new and existing shareholders following its Analyst and Investor Research Webcast in September 2021.

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 third 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: 6995569. 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; 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; 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 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; 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)

	September 30, 2021	December 31, 2020

Assets		
Current assets:		
Cash and cash equivalents	$ 123,896	$ 184,497
Accounts receivable	22,500	30,000
Prepaid expenses	7,627	10,434
Other current assets	3,964	5,111
Total current assets	157,987	230,042
Long-term assets:		
Property and equipment, net	24,020	29,198
Operating lease right-of-use assets	14,639	16,232
Restricted cash	3,651	3,651
Other assets	215	115
Total long-term assets	42,525	49,196
Total assets	$ 200,512	$ 279,238
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 7,443	$ 13,795
Accrued expenses and other current liabilities	11,364	11,971
Current portion of deferred revenue	8,736	91,560
Current portion of operating lease liability	4,097	3,714
Total current liabilities	31,640	121,040
Long-term liabilities:		
Deferred revenue, net of current portion	107,606	41,481
Operating lease liability, net of current portion	22,477	25,591
Other liabilities	1,014	474
Total long-term liabilities	$ 131,097	$ 67,546
Total liabilities	$ 162,737	$ 188,586
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at September 30, 2021 and December 31, 2020	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 51,998,032 and 48,778,678 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively	$ 716,118	$ 694,085
Additional paid-in capital	84,254	71,573
Accumulated other comprehensive income	258	389
Accumulated deficit	(770,729)	(683,269)
Total shareholders' equity	$ 29,901	$ 82,778
Total liabilities, Series A preferred shares and shareholders' equity	$ 200,512	$ 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenue	$ 36,423	$ 3,450	$ 39,199	$ 10,638
Operating expenses:				
Research and development	31,086	28,275	96,114	100,911
General and administrative	12,944	9,590	33,991	32,791
Total operating expenses	44,030	37,865	130,105	133,702
Loss from operations	(7,607)	(34,415)	(90,906)	(123,064)
Other income, net:				
Dividend income and interest income, net	6	23	25	544
Other income, net	1,371	1,292	3,421	1,399
Total other income, net	1,377	1,315	3,446	1,943
Loss before income taxes	(6,230)	(33,100)	(87,460)	(121,121)
Income tax provision	—	—	—	—
Net loss	$ (6,230)	$ (33,100)	$ (87,460)	$ (121,121)

Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.12)	$ (0.86)	$ (1.75)	$ (3.36)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	50,709,877	38,364,224	50,017,521	36,021,256
Other comprehensive income (loss):				
Net loss	$ (6,230)	$ (33,100)	$ (87,460)	$ (121,121)
Foreign currency translation	(11)	23	(131)	34
Comprehensive loss	$ (6,241)	$ (33,077)	$ (87,591)	$ (121,087)

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