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

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Dosing underway in FOCUS-C9 clinical trial of WVE-004 in C9-ALS / C9-FTD – first oligonucleotide using PN backbone chemistry modifications in clinical study

Recruitment ongoing for clinical trials in HD and DMD

Generating clinical data in multiple trials through 2022 to enable decision making

Leading endogenous ADAR editing capability demonstrated restoration of functional AAT protein in vivo; new data at Wave Research Day September 28

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

CAMBRIDGE, Mass., Aug. 05, 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 second quarter ended June 30, 2021 and provided a business update.

“Since the start of the second quarter, Wave has achieved two significant milestones: the intrathecal dosing of patients with an oligonucleotide containing PN chemistry and preclinical proof-of-concept protein restoration *in vivo* with ADAR editing for our alpha-1 antitrypsin deficiency program. Both accomplishments reflect the significant evolution of our PRISM platform since Wave’s founding,” said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. “Amyotrophic lateral sclerosis and frontotemporal dementia are both areas of high unmet need; therefore we are excited to advance WVE-004 in the FOCUS-C9 clinical trial, which is open to both patient populations as they have the same genetic cause of disease. Additionally, we continue to progress our clinical trials for Huntington’s disease and Duchenne muscular dystrophy. Our novel PN chemistry, stereochemical control and years of platform learnings have enabled us to lead the field on RNA editing and develop a best-in-class modality using endogenous ADAR enzymes, which further expands our genetic medicines toolkit. In June we delivered our first preclinical proof-of-concept data for our AATD program, and we believe RNA editing is the ideal approach to address this disease. Our upcoming Analyst and Investor Research Day in September will feature new data on our ADAR editing capability, AATD program, and updates on applications of ADAR editing beyond liver, including in the CNS.”

Highlights and upcoming milestones for clinical silencing and exon skipping programs:

WVE-004 for C9orf72-associated amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (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).

Clinical trial update:

- In July 2021, Wave announced the initiation of dosing in the Phase 1b/2a FOCUS-C9 clinical trial of WVE-004 in C9orf72-associated ALS and FTD.
- The FOCUS-C9 trial is adaptive, with dose escalation and dosing frequency being guided by an independent committee.
- Wave expects to generate clinical data through 2022 to provide insight into the clinical effects of PN chemistry and enable decision making for WVE-004.

Presentations and preclinical data:

- In the second quarter, Wave highlighted preclinical *in vivo* data for WVE-004 at multiple scientific meetings:
  - American Academy of Neurology (AAN) 2021 Virtual Annual Meeting in April 2021
  - European Network to Cure ALS (ENCALS) in May 2021
  - Keystone eSymposia: Neurodegenerative Diseases: Genes, Mechanisms and Therapeutics in June 2021
- The preclinical *in vivo* data for WVE-004 demonstrated potent knockdown of more than 90% of polyGP dipeptide repeat (DPR) proteins in the spinal cord and at least 80% in the cortex of a transgenic mouse model, which was durable out to at least six months. C9orf72 protein was relatively unchanged over the same time period.
- At Keystone eSymposia, Wave also shared preclinical data demonstrating the impact of applying PN chemistry to WVE-004, which resulted in improved activity and durability *in vivo* in both spinal cord and cortex compared with a control molecule of the same sequence designed without PN chemistry.

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

- WVE-003 is Wave's next-generation stereopure HD candidate and first HD candidate to use PN chemistry and leverage transgenic models to assess target engagement *in vivo.*
- WVE-003 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, 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 compared to 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.
- Preclinical data for WVE-003 demonstrated selective reduction of mHTT mRNA *in vitro* and potent and durable knockdown of mHTT mRNA *in vivo*.
- Sites are activated and recruitment is underway in the SELECT-HD Phase 1b/2a clinical trial of WVE-003 in patients with early manifest HD, and Wave expects to initiate dosing in 2021. SELECT-HD is adaptive, with dose escalation and dosing frequency to be guided by an independent committee.

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

- WVE-N531 is Wave's first stereopure splicing candidate to incorporate PN chemistry, which Wave advanced following results of an *in vivo* study in double knock-out mice (dKO) that showed 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.
- Sites are activated and recruitment is underway in a clinical trial of WVE-N531 in patients with DMD amenable to exon 53 skipping. Wave expects to initiate dosing in 2021.

ADAR editing preclinical program progress and upcoming milestones:

ADAR editing (RNA editing using endogenous ADAR enzymes) capability:

- Wave's leading RNA editing capability leverages widely expressed endogenous ADAR enzymes to achieve highly specific A-to-I (G) RNA editing *in vivo* using stereopure oligonucleotides, without the need for lipid nanoparticles (LNPs) or AAV vectors and without altering DNA.
- In May 2021, at the 24th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), Wave presented its novel ADAR editing capability, which leverages PN chemistry. This presentation highlighted proof-of-concept data demonstrating potent and durable editing of ACTB *in vivo* in the liver of non-human primates (NHPs) of up to 50% using GalNAc-conjugated oligonucleotides, as well as potent editing of ACTB *in vivo* in multiple tissues of NHPs using non-conjugated oligonucleotides. The presentation also included data demonstrating potent editing *in vivo* in the CNS with Wave's proprietary humanized ADAR transgenic mouse model.
- Wave continues to evaluate ADAR editing oligonucleotides for different disease targets, including neurology targets, leveraging its proprietary mouse model.
- Wave expects to present additional ADAR editing data at its upcoming Analyst and Investor Research Day on September 28, 2021, and at scientific congresses in 2021.

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. ADAR editing may provide an ideal approach to addressing AATD by increasing circulating levels of healthy alpha-1 antitrypsin (M-AAT) protein and reducing aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.
- In June 2021, Wave presented proof-of-concept preclinical *in vivo* data that demonstrated up to 40% editing of human *SERPINA1* Z allele mRNA in the liver at an initial timepoint, which resulted in a therapeutically meaningful increase in circulating, functional wild-type AAT protein. This initial *in vivo* study utilized Wave's proprietary transgenic mouse model, which has both the human *SERPINA1* Z-allele as well as human ADAR that is expressed comparably to human cells. These data have been accepted for an oral presentation at the 17th Annual Meeting of the Oligonucleotide Therapeutics Society (OTS) being held September 26 – 29, 2021.
- Wave's preclinical studies for its AATD program are ongoing and additional data on durability and dose response are expected in the second half of 2021.

Preclinical CNS programs in collaboration with Takeda:

Multiple programs (including WVE-005) for central nervous system (CNS) indications:

- Wave is utilizing PN chemistry 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, including target engagement in the CNS of non-human primates, and progress multiple discovery programs towards portfolio entry and candidate nomination.

Upcoming events:

Analyst and Investor Research Day to be held September 28, 2021:

- Wave announced today it will hold an Analyst and Investor Research Day on Tuesday, September 28th, at 10:00 a.m. ET to discuss its PRISM™ platform, share new preclinical data from its neurology programs and proof-of-concept data for its ADAR editing capability, and provide an update on its first ADAR editing program for AATD.

Second Quarter 2021 Financial Results and Financial Guidance

Wave reported a net loss of $38.8 million in the second quarter of 2021 as compared to $40.5 million in the same period in 2020.

Research and development expenses were $31.6 million in the second quarter of 2021 as compared to $31.5 million in the same period in 2020. While the total research and development expenses remained relatively consistent year-over-year, there were changes in how the expenses were distributed between programs. There were increased external expenses related to Wave's C9orf72 program and other discovery and development programs, including PRISM, and Wave's reimbursed research and preclinical expenses related to its Takeda collaboration. These increases were almost entirely offset by decreased external expenses related to Wave's discontinued clinical programs.

General and administrative expenses were $11.0 million in the second quarter of 2021 as compared to $10.2 million in the same period in 2020. The increase in general and administrative expenses in the second quarter of 2021 was mainly driven by increased external general and administrative expenses, as well as increased compensation-related expenses.

As of June 30, 2021, Wave had $143.8 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 $81.2 million, partially offset by the receipt of $30.0 million in research support funding from Takeda under the company's collaboration in the second quarter and $13.1 million in year-to-date net proceeds under Wave's 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 8:30 a.m. ET to discuss the company's second quarter and 2021 financial results and provide a business update. The conference call may be accessed by dialing (800) 708-4540 (domestic) or (847) 619-6397 (international) and entering conference ID: 50197439. 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, 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)

	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 143,840	$ 184,497
Current portion of accounts receivable	—	30,000
Prepaid expenses	9,188	10,434
Other current assets	6,403	5,111
Total current assets	159,431	230,042
Long-term assets:		
Property and equipment, net	25,842	29,198
Operating lease right-of-use assets	15,189	16,232
Restricted cash	3,651	3,651
Other assets	2,298	115
Total long-term assets	46,980	49,196
Total assets	$ 206,411	$ 279,238
Liabilities, Series A preferred shares and shareholders’ equity		
Current liabilities:		
Accounts payable	$ 8,655	$ 13,795
Accrued expenses and other current liabilities	9,923	11,971
Current portion of deferred revenue	24,177	91,560
Current portion of operating lease liability	3,966	3,714
Total current liabilities	46,721	121,040
Long-term liabilities:		
Deferred revenue, net of current portion	106,088	41,481
Operating lease liability, net of current portion	23,547	25,591
Other liabilities	339	474
Total long-term liabilities	$ 129,974	$ 67,546
Total liabilities	$ 176,695	$ 188,586
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at June 30, 2021 and December 31, 2020	$ 7,874	$ 7,874
Shareholders’ equity:		
Ordinary shares, no par value; 50,576,466 and 48,778,678 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively	$ 707,714	$ 694,085
Additional paid-in capital	78,358	71,573
Accumulated other comprehensive income	269	389
Accumulated deficit	(764,499)	(683,269)
Total shareholders’ equity	$ 21,842	$ 82,778
Total liabilities, Series A preferred shares and shareholders’ equity	$ 206,411	$ 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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenue	$ 2,776	$ 3,027	$ 2,776	$ 7,188
Operating expenses:				

Research and development	31,635	31,478	65,028	72,636
General and administrative	10,969	10,205	21,047	23,201
Total operating expenses	42,604	41,683	86,075	95,837
Loss from operations	(39,828)	(38,656)	(83,299)	(88,649)
Other income (expense), net:				
Dividend income and interest income, net	8	133	19	521
Other income (expense), net	1,054	(2,005)	2,050	107
Total other income (expense), net	1,062	(1,872)	2,069	628
Loss before income taxes	(38,766)	(40,528)	(81,230)	(88,021)
Income tax provision	—	—	—	—
Net loss	$ (38,766)	$ (40,528)	$ (81,230)	$ (88,021)
Net loss per share attributable to ordinary shareholders —basic and diluted	$ (0.78)	$ (1.15)	$ (1.65)	$ (2.53)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	49,973,185	35,212,291	49,220,140	34,836,898
Other comprehensive income (loss):				
Net loss	$ (38,766)	$ (40,528)	$ (81,230)	$ (88,021)
Foreign currency translation	—	5	(120)	11
Comprehensive loss	$ (38,766)	$ (40,523)	$ (81,350)	$ (88,010)

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