Wave Life Sciences Reports Second Quarter 2022 Financial Results and Provides Business Update

August 11, 2022

WVE-006 announced as investigational development candidate for AATD with CTA submissions expected in 2023; first-in-class RNA editing candidate and most advanced program currently in development using an oligonucleotide to harness an endogenous enzyme for editing

Data for ongoing clinical programs, including WVE-004, WVE-003, and WVE-N531, expected in 2H 2022

Positive target engagement data in C9-ALS/FTD with single low doses of WVE-004 highlighted at ENCALS conference

$70 million financing in June 2022 strengthened balance sheet and extended cash runway to the end of 2023

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

CAMBRIDGE, Mass., Aug. 11, 2022 (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, 2022 and provided a business update.

"At Wave, we are urgently working to advance our lead programs for the treatment of devastating genetic diseases. Since the start of the second quarter of 2022, we have achieved multiple important milestones, including positive target engagement data in our FOCUS-C9 clinical trial and the selection of our first RNA editing, or 'AIMer', development candidate, WVE-006 for the treatment of AATD," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "RNA editing is a novel therapeutic modality and Wave is leading this field with our AIMers. These RNA base editing therapeutics are being advanced with and without GalNAc conjugation and avoid the need for large, complex delivery vehicles, such as lipid nanoparticles or viral vectors. Our recent financing ensures we are well-capitalized to execute on several key milestones, including data announcements from three ongoing clinical trials and the advancement of WVE-006 into clinical development."

Recent Pipeline and Business Highlights

Alpha-1 antitrypsin deficiency clinical candidate (WVE-006) selected; program designed to correct mutant AATD transcript to address both liver and lung manifestations of disease

- Today, Wave announced WVE-006, its PN-modified GalNAc-conjugated development candidate for the treatment of alpha-1 antitrypsin deficiency (AATD) and its first ever AIMer (A-to-I(G) RNA base editing oligonucleotide) development candidate. WVE-006 is a first-in-class RNA editing candidate and the most advanced program currently in development using an oligonucleotide to harness an endogenous enzyme for editing.
- Preclinical studies with WVE-006 suggest potential for a best-in-class treatment for AATD and IND-enabling activities for WVE-006 are underway.
- The Company expects to submit clinical trial applications (CTAs) for WVE-006 in 2023.

FOCUS-C9 clinical trial of WVE-004 for C9-ALS and C9-FTD continues to advance; previously announced positive target engagement data highlighted at ENCALS meeting

- In June 2022, Wave presented positive target engagement data from the company's ongoing FOCUS-C9 clinical trial of WVE-004 (PN-modified variant selective silencing oligonucleotide) for C9orf72-associated amyotrophic lateral sclerosis (C9-ALS) and frontotemporal dementia (C9-FTD) as an oral presentation at the European Network to Cure ALS (ENCALS) meeting in Edinburgh, Scotland. These data, which were first announced in April 2022, demonstrate potent and durable target engagement after participants received a low, single dose of WVE-004.
- In April 2022, Wave announced the publication of preclinical data for WVE-004 in C9-ALS and C9-FTD in the journal *Molecular Therapy Nucleic Acids* demonstrating that WVE-004 potently reduces C9orf72 transcriptional variants and poly(GP) dipeptide repeat proteins in mice for at least six months while maintaining C9orf72 protein levels. The paper, titled "Preclinical evaluation of WVE-004, an investigational stereopure antisense oligonucleotide for the treatment of C9orf72-associated ALS or FTD," is available here.
- FOCUS-C9 (NCT04931862) is an adaptive clinical trial that is designed to rapidly optimize dose level and frequency based on early indicators of target engagement. WVE-004 is designed to selectively target transcript variants containing a hexanucleotide repeat expansion (G_4C_2) associated with the C9orf72 gene for the treatment of C9-ALS and C9-FTD, thereby reducing pathological mRNA products and toxic DPR proteins, including poly(GP).

SELECT-HD clinical trial for WVE-003 in Huntington's disease (HD) continues to advance; only allele-selective clinical program designed to reduce mutant HTT and spare healthy HTT

- WVE-003 for HD (PN-modified allele-selective silencing oligonucleotide) is being evaluated in the ongoing, adaptive, double-blind Phase 1b/2a SELECT-HD clinical trial (NCT05032196). WVE-003 is the only compound in clinical development designed to selectively lower mutant HTT (mHTT) protein levels, while leaving wild-type (healthy) HTT (wtHTT) protein levels relatively intact.
- Based upon review of blinded CSF concentrations of WVE-003 from the SELECT-HD clinical trial, CSF concentrations of

WVE-003 observed in HD patients following single doses of WVE-003 were at levels expected to engage target and substantially higher than those achieved following the highest doses of WVE-120101 (SNP1) and WVE-120102 (SNP2), Wave's first-generation PS/PO silencing compounds previously evaluated in the clinic. This observation once again illustrates the impact of Wave's next-generation chemistry on the pharmacological profile compared with its first-generation compounds.

Phase 1b/2a clinical trial of WVE-N531 in Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping continues to advance; dosing underway at fourth dose level

- WVE-N531 for DMD (PN-modified splicing oligonucleotide) is being evaluated in an open-label, intra-patient dose escalation clinical trial (NCT04906460). Dose escalation is ongoing and being guided by tolerability and plasma PK, with possible cohort expansion informed by an assessment of drug distribution in muscle and biomarkers, including dystrophin, following multiple doses of WVE-N531.
- Dosing in boys with DMD amenable to exon 53 skipping is underway at dose levels comparable to the human equivalent of those explored preclinically in the double knock-out (dKO) mouse model where a surrogate of WVE-N531 substantially improved survival. Plasma concentrations and half-life of WVE-N531 observed in the patients enrolled in Wave's ongoing clinical trial were significantly greater than plasma concentrations achieved following the highest doses of suvodirsen, Wave's first-generation PS/PO exon-skipping compound administered in Phase 2/3 studies.

Extended cash runway with successful financing

- In June 2022, Wave closed an underwritten offering with existing investors for the issuance and sale of ordinary shares and pre-funded warrants with gross proceeds of approximately $70.0 million. With this additional capital, Wave strengthened its balance sheet and extended its cash runway to the end of 2023.

Key Anticipated Upcoming Milestones

WVE-006 (GalNAc-conjugated AIMer) for AATD:

- Wave expects to submit clinical trial applications for WVE-006 in 2023.

WVE-004 for C9-ALS and C9-FTD:

- Additional single and multidose clinical data for WVE-004 expected in 2H 2022. Wave expects to use these data to optimize WVE-004 dose level and frequency, as well as to enable discussions with regulatory authorities regarding the next phase of development later in 2022.
- Planning underway to initiate an open-label extension (OLE) clinical trial in 2H 2022.

WVE-003 for HD:

- Clinical data expected in 2H 2022 for WVE-003 to provide further insight into the clinical effects of PN chemistry and enable decision-making for this program.

WVE-N531 for DMD:

- Clinical data, including muscle biopsies, expected in 4Q 2022 for WVE-N531 to provide further insight into the clinical effects of PN chemistry and enable decision-making for this program.

Recent Scientific Publications

- Wave has published a total of eight peer-reviewed papers thus far in 2022. All of Wave's publications can be viewed here.

Second Quarter 2022 Financial Results and Financial Guidance
Wave reported a net loss of $41.3 million in the second quarter of 2022, as compared to $38.8 million in the same period in 2021.

Wave recorded revenue of $0.4 million for the second quarter of 2022, as compared to $2.8 million in the same period in 2021.

Research and development expenses were $29.7 million in the second quarter of 2022 as compared to $31.6 million in the same period in 2021. The decrease in research and development expenses in the second quarter was primarily due to decreased external expenses related to our previously disclosed discontinued PRECISION-HD programs, partially offset by increased share-based compensation expense and increased external expenses related to AATD.

General and administrative expenses were $12.8 million in the second quarter of 2022 as compared to $11.0 million in the same period in 2021. The increase in general and administrative expenses in the second quarter of 2022 was primarily due to increases in compensation-related expenses, primarily from share-based compensation, offset by decreases in other external general and administrative expenses.

As of June 30, 2022, Wave had $148.2 million in cash, cash equivalents and short-term investments. As of December 31, 2021, Wave had $150.6 million in cash and cash equivalents. The net decrease is primarily due to Wave's year to date operating cash burn, partially offset by $65.5 million net proceeds from its financing in June.

Wave expects that its existing cash, cash equivalents and short-term investments will enable the company to fund its operating and capital expenditure requirements to the end 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 2022 financial results and

provide a business update. The webcast of the conference call may be accessed by visiting “Events” on the investor relations section of the Wave Life Sciences corporate website: ir.wavelifesciences.com/events-and-presentations.

Analysts planning to participate during the Q&A portion of the live call can join the conference call at the following audio conferencing link: available here. It is recommended that participants register at least 15 minutes in advance of the call. Once registered, participants will receive the dial-in information.

Following the live event, an archived version of the webcast will be available on the Wave Life Sciences website.

About the FOCUS-C9 Clinical Trial
The FOCUS-C9 trial is an ongoing, global, multicenter, randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial to assess the safety and tolerability of single- and multiple-ascending intrathecal doses of WVE-004 for people with C9-ALS and/or C9-FTD. Additional objectives include measurement of poly(GP) DPR proteins in the cerebrospinal fluid (CSF), plasma and CSF pharmacokinetics (PK), and exploratory biomarkers and clinical outcomes. The FOCUS-C9 trial is designed to be adaptive, with dose escalation and dosing frequency being guided by an independent committee.

In an initial data analysis, reductions in poly(GP) were observed across all active treatment groups (10 mg, n=2 patients; 30 mg, n=4 patients; 60 mg, n=3 patients), reaching statistical significance versus placebo (n=3 patients) after single 30 mg doses, with a 34% reduction in poly(GP) at day 85 (p=0.011). At the time of analysis, none of the patients dosed with 60 mg had reached day 85. As the poly(GP) reduction in the 30 mg single dose cohort does not appear to have plateaued, Wave will extend the observation period from approximately three months (85 days) to approximately six months to identify the maximum reduction of poly(GP) and duration of effect of low single doses. Based on the durability and potency observed in the 30 mg cohort, FOCUS-C9 has been adapted to include additional patients receiving 20 mg and 30 mg single doses of WVE-004. Adverse events (AEs) were balanced across treatment groups, including placebo, and were mostly mild to moderate in intensity. Four patients (including one on placebo) experienced severe and/or serious adverse events; three were reported by the investigators to be related to ALS or administration, and one was reported by the investigator to be related to study drug. There were no treatment-associated elevations in CSF white blood cell counts or protein and no other notable laboratory abnormalities were observed.

Support for FOCUS-C9 is provided by the Alzheimer’s Drug Discovery Foundation.

About Amyotrophic Lateral Sclerosis and Frontotemporal Dementia
Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease in which the progressive degeneration of motor neurons in the brain and spinal cord leads to the inability to initiate or control muscle movement. People with ALS may lose the ability to speak, eat, move and breathe. ALS affects as many as 20,000 people in the United States.

Frontotemporal dementia (FTD) is a fatal neurodegenerative disease in which progressive nerve cell loss in the brain's frontal lobes and temporal lobes leads to personality and behavioral changes, as well as the gradual impairment of language skills. It is the second most common form of early-onset dementia after Alzheimer’s disease in people under the age of 65. FTD affects as many as 70,000 people in the United States.

A hexanucleotide repeat expansion (G_4C_2) is the most common known genetic cause of the sporadic and inherited forms of ALS and FTD. The expansion leads to production of modified sense and antisense transcripts that can form nuclear RNA foci and encode dipeptide protein repeats (DPRs), which are believed to drive disease pathology. Additionally, the G_4C_2 expansion can decrease expression of C9orf72 protein, affecting regulation of neuronal function and the immune system.

In the United States, mutations of the C9orf72 gene are present in approximately 40% of familial ALS cases and ~8-10% of sporadic ALS cases. In FTD, the mutations appear in 38% of familial cases and 6% of sporadic cases.

About Huntington’s Disease
Huntington’s disease (HD) is a debilitating and ultimately fatal autosomal dominant neurological disorder, characterized by cognitive decline, psychiatric illness, and chorea. HD causes nerve cells in the brain to deteriorate over time, affecting thinking ability, emotions, and movement. HD is caused by an expanded cytosine-adenine-guanine (CAG) triplet repeat in the huntingtin (HTT) gene that results in production of mutant HTT (mHTT) protein. Accumulation of mHTT causes progressive loss of neurons in the brain. Wild-type, or healthy, HTT (wtHTT) protein is critical for neuronal function and suppression may have detrimental long-term consequences. Approximately 30,000 people in the United States have symptomatic HD and more than 200,000 others are at risk for developing the disease. There are currently no approved disease-modifying therapies available.

About Duchenne Muscular Dystrophy
Duchenne muscular dystrophy (DMD) is a fatal X-linked genetic neuromuscular disorder caused predominantly by out-of-frame deletions in the dystrophin gene, resulting in absent or defective dystrophin protein. Dystrophin protein is needed for normal muscle maintenance and operation. Because of the genetic mutations in DMD, the body cannot produce functional dystrophin, which results in progressive and irreversible loss of muscle function, including the heart and lungs. Worldwide, DMD affects approximately one in 5,000 newborn boys. Approximately 8%-10% of DMD patients have mutations amenable to treatment with an exon 53 skipping therapy. Exon skipping aims to address the underlying cause of DMD by promoting the production of dystrophin protein to stabilize or slow disease progression

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 and completion of our adaptive clinical trials, and the announcement of

such events; the protocol, design and endpoints of our ongoing and future 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 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 approach; 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 status and progress of our novel programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; 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; the clinical results of our programs and the timing thereof, which may not support further development of product candidates; actions of regulatory agencies and their receptiveness to our adaptive trial designs, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing regulatory interactions and future clinical trials; 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; 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; our ability to maintain the company infrastructure and personnel needed to achieve our goals; the severity and duration of the COVID-19 pandemic and variants thereof, 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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 123,163	$ 150,564
Short-term investments	25,000	—
Prepaid expenses	5,396	6,584
Other current assets	6,555	5,416
Total current assets	160,114	162,564
Long-term assets:		
Property and equipment, net	19,808	22,266
Operating lease right-of-use assets	28,791	18,378
Restricted cash	3,651	3,651
Other assets	955	148
Total long-term assets	53,205	44,443
Total assets	$ 213,319	$ 207,007
Liabilities, Series A preferred shares and shareholders’ equity		
Current liabilities:		
Accounts payable	$ 11,168	$ 7,281
Accrued expenses and other current liabilities	11,085	14,861
Current portion of deferred revenue	37,466	37,098
Current portion of operating lease liability	4,363	4,961
Total current liabilities	64,082	64,201
Long-term liabilities:		
Deferred revenue, net of current portion	75,256	77,479
Operating lease liability, net of current portion	35,160	24,955
Total long-term liabilities	110,416	102,434
Total liabilities	$ 174,498	$ 166,635
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at June 30, 2022 and December 31, 2021	$ 7,874	$ 7,874
Shareholders’ equity:		
Ordinary shares, no par value; 86,724,658 and 59,841,116 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively	$ 802,449	$ 749,851
Additional paid-in capital	113,169	87,980
Accumulated other comprehensive income (loss)	(47)	181
Accumulated deficit	(884,624)	(805,514)
Total shareholders’ equity	$ 30,947	$ 32,498
Total liabilities, Series A preferred shares and shareholders’ equity	$ 213,319	$ 207,007

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,	
	2022	**2021**	**2022**	**2021**
Revenue	$ 375	$ 2,776	$ 2,125	$ 2,776
Operating expenses:				
Research and development	29,733	31,635	57,203	65,028
General and administrative	12,806	10,969	25,180	21,047
Total operating expenses	42,539	42,604	82,383	86,075
Loss from operations	(42,164)	(39,828)	(80,258)	(83,299)
Other income, net:				
Dividend income and interest income, net	124	8	150	19
Other income, net	744	1,054	998	2,050
Total other income, net	868	1,062	1,148	2,069
Loss before income taxes	(41,296)	(38,766)	(79,110)	(81,230)
Income tax provision	—	—	—	—
Net loss	$ (41,296)	$ (38,766)	$ (79,110)	$ (81,230)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.62)	$ (0.78)	$ (1.25)	$ (1.65)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	66,479,293	49,973,185	63,514,426	49,220,140
Other comprehensive loss:				
Net loss	$ (41,296)	$ (38,766)	$ (79,110)	$ (81,230)
Foreign currency translation	(142)	—	(228)	(120)
Comprehensive loss	$ (41,438)	$ (38,766)	$ (79,338)	$ (81,350)

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