Wave Life Sciences Reports Second Quarter 2024 Financial Results and Provides Business Update

August 8, 2024

Successful clinical translation of Wave's RNA medicines platform in HD patients with WVE-003 provides further validation of Wave's proprietary platform with PN and stereochemistry; opt-in package for WVE-003 submitted to partner Takeda and engagement with regulators initiated to discuss potential path to accelerated approval

Dystrophin data on track for 3Q 2024 from potentially registrational FORWARD-53 trial of WVE-N531, which has previously demonstrated industry-leading exon skipping of 53%; positive data would unlock a best-in-class functional dystrophin franchise for DMD

Dosing initiated in 3Q 2024 in RestorAATion-2 clinical trial of WVE-006 in AATD patients; proof-of-mechanism data in AATD patients expected in 4Q 2024

New preclinical data supporting INHBE siRNA (WVE-007) as a potential best-in-class treatment for obesity, as well as new data from Wave's wholly owned pipeline of RNA medicines, expected at R&D Day in Fall 2024

Investor conference call and webcast at 8:30 a.m. ET today

CAMBRIDGE, Mass., Aug. 08, 2024 (GLOBE NEWSWIRE) -- Wave Life Sciences Ltd. (Nasdaq: WVE), a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health, today announced financial results for the second quarter ended June 30, 2024, and provided a business update.

"With our recent positive SELECT-HD trial results, we have further validated our chemistry and the clinical translation of our platform. Today, we have built an RNA medicines platform that is positioned to sustainably translate clinical genetic insights into transformational medicines as we continue to advance our lead programs through multiple important milestones in the second half of this year," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Clinical results from our SELECT-HD trial in HD demonstrated statistically significant, potent, and durable allele-selective silencing with WVE-003, and we are working rapidly to engage regulators on a potential path to accelerated approval. These data have also bolstered our confidence ahead of expected upcoming readouts from our potentially registrational FORWARD-53 trial in DMD and our RestorAATion-2 trial in AATD. In parallel with these efforts, we continue to drive our best-in-class obesity candidate, WVE-007, toward the clinic and are on track to initiate the first-in-human study in the first quarter of next year. We look forward to providing additional updates on our growing, high-value pipeline and our progress towards reimagining what's possible for human health at our R&D Day this Fall."

Recent Business Highlights

HD (allele-selective silencing)

- **WVE-003** is a first-in-class, allele-selective oligonucleotide designed to lower mutant huntingtin (mHTT) protein and preserve healthy, wild-type huntingtin (wtHTT) protein, a protein critical to the health of the central nervous system. As compared to non-selective HTT lowering approaches, WVE-003 is uniquely positioned to address presymptomatic HD patients, as well as symptomatic patients. There are currently no disease modifying therapies for HD, which affects over 200,000 individuals across pre-symptomatic and symptomatic disease stages in the US and Europe. WVE-003 is expected to address approximately 40% of the HD population, and up to 80% of HD patients may be addressed in the future with other SNP-targeted candidates.
- In June, Wave announced positive clinical data from the Phase 1b/2a SELECT-HD study of WVE-003. Results from the multi-dose (three doses every eight weeks) portion showed clear translation of target engagement to clinic with statistically significant, potent, durable and allele-selective reductions in CSF mHTT of up to 46% and preservation of healthy protein. This cohort also revealed a statistically significant correlation between mHTT reductions and slowing of caudate atrophy, indicating a potential benefit of allele-selective mHTT reductions. Structural brain MRI changes, such as caudate atrophy, are well-characterized measures of disease progression and neurodegeneration in HD. WVE-003 was generally safe and well-tolerated, with mild-to-moderate adverse events and no Serious Adverse Events.
- Wave has submitted its opt-in package to its partner, Takeda, and initiated engagement with regulators on a clinical development path to accelerated approval.
- **Expected upcoming milestone:** Wave expects a decision from Takeda on their option right, as well as feedback from regulators on a clinical development path to accelerated approval by year-end.

DMD (exon skipping)

- **WVE-N531** is an exon-skipping oligonucleotide designed to induce production of endogenous, functional dystrophin protein for the treatment of boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. In a previously completed study (three doses every other week), WVE-N531 achieved industry-leading mean exon skipping levels of 53%, mean muscle tissue concentrations of ~42,000 ng/g, and distribution to myogenic stem cells (also known as satellite cells) in all study participants.
- Wave continues to advance FORWARD-53, a potentially registrational, open-label clinical trial of 11 boys with DMD, which is evaluating WVE-N531 administered every-other-week. Endpoints include dystrophin expression after 24 and 48 weeks of treatment, as well as pharmacokinetic, safety and tolerability data.

- Pending positive results from the FORWARD-53 trial, the company is planning to advance a broader DMD pipeline of PN-modified oligonucleotides for skipping other exons, with the goal of providing new and best-in-class treatment options for a larger population of boys with DMD.
- In 2023, exon skipping therapeutics for DMD achieved approximately ~$1 billion in sales, primarily in the US, across exons covering approximately ~29% of the DMD population. WVE-N531 could address up to 10% of the DMD population, which encompasses over 2,000 boys in the US and Europe; and with the addition of other exons, Wave could address up to 40% of the DMD population.
- **Expected upcoming milestone:** Wave expects to deliver data, including dystrophin protein expression from muscle biopsies after 24 weeks of treatment, in the third quarter of 2024.

AATD (GalNAc-RNA editing)

- **WVE-006** is a GalNAc-conjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that is uniquely designed to address AATD-related lung disease, liver disease, or both. WVE-006 does not use a lipid-nanoparticle (LNP) delivery system. WVE-006 is currently being evaluated in the RestorAATion-2 Phase 1b/2a study in Pi*ZZ patients with AATD.
- There are an estimated 200,000 Pi*ZZ patients in the US and Europe. Treatment options are currently limited to weekly IV augmentation therapy for lung disease only (representing over $1 billion in world-wide sales in 2023). There are no approved therapies to address AATD liver disease, which ultimately requires many patients to undergo liver transplantation.
- In the third quarter of 2024, Wave initiated dosing in the single dose portion of the first dose cohort of RestorAATion-2, at a dose level expected to engage target, meaning inducing RNA editing, based on preclinical data.
- **Expected upcoming milestone:** Wave expects to deliver proof-of-mechanism data from RestorAATion-2 in patients with AATD in the fourth quarter of 2024.

Obesity (GalNAc-siRNA)

- **WVE-007** is a GalNAc-conjugated small interfering RNA (GalNAc-siRNA) that is designed to silence the INHBE (Inhibin βE) gene to induce lipolysis (fat-burning) while preserving muscle mass to restore and maintain a healthy metabolic profile thereby recapitulating the protective effects of INHBE loss-of-function (LoF) mutations. Heterozygous INHBE LoF carriers, identified through multiple large human genetic databases including UK Biobank, have a favorable cardiometabolic profile, including reduced abdominal obesity and reduced odds of type 2 diabetes and coronary artery disease.
- WVE-007 has potential to address obesity as a front-line monotherapy, in combination with GLP-1s for further improvement of weight loss or to reduce the doses of GLP-1s, or as a maintenance therapy following cessation of GLP-1s.
- In preclinical mouse models, Wave's INHBE GalNAc-siRNA has demonstrated highly potent (ED50 < 1mg/kg) and durable silencing following one, low-single-digit dose, supporting every-six-month or annual subcutaneous dosing in humans. Preclinical data also demonstrated weight loss similar to semaglutide, with no loss of muscle mass and a reduction in fat mass with preferential effects on visceral fat, consistent with the profile of INHBE LoF carriers in human genetics.
- In a separate ongoing study in DIO mice, when administered in combination with semaglutide, a single dose of Wave's INHBE GalNAc-siRNA doubled the weight loss observed with semaglutide alone and this effect was sustained throughout the duration of the study. As previously reported, treatment with Wave's INHBE GalNAc-siRNA upon cessation of semaglutide treatment curtailed expected rebound weight gain. The company plans to share additional preclinical data later this year.
- **Expected upcoming milestone:** Wave expects to initiate a clinical trial for WVE-007 in the first quarter of 2025.

RNA Medicines Platform and Pipeline Expansion

- Wave plans to hold an R&D Day in Fall 2024 which will highlight its innovations in chemistry and pipeline of transformative RNA medicines, as well as new preclinical data from Wave's wholly owned portfolio of candidates, including WVE-007 (INHBE siRNA).
- Wave continues to advance its pipeline of wholly owned RNA therapeutics across a range of high-impact GalNAc-hepatic and extra-hepatic targets. Powered by genetic datasets and deep learning models, Wave is also utilizing its proprietary "edit-verse" to identify new RNA editing targets that leverage easily accessible biomarkers, offer efficient paths to proof-of-concept in humans, address diseases of high unmet need, and represent meaningful commercial opportunities.

Financial Highlights

- Cash and cash equivalents were $154.0 million as of June 30, 2024, compared to $200.4 million as of December 31, 2023. Wave expects that its current cash and cash equivalents will be sufficient to fund operations into the fourth quarter of 2025. Potential future milestone and other payments to Wave under its GSK and Takeda collaborations are not included in its cash runway.
- Revenue was $19.7 million for the second quarter of 2024, as compared to $22.1 million in the second quarter of 2023.
- Research and development expenses were $40.4 million in the second quarter of 2024, as compared to $33.3 million in the second quarter of 2023. General and administrative expenses were $14.3 million in the second quarter of 2024, as compared to $12.3 million in the second quarter of 2023.
- Net loss was $32.9 million for the second quarter of 2024, as compared to $21.1 million for the second quarter of 2023.

Investor Conference Call and Webcast

Wave will host an investor conference call today at 8:30 a.m. ET to review the second quarter 2024 financial results and pipeline updates. A webcast of the conference call can be accessed by visiting "Investor Events" on the investor relations section of the Wave Life Sciences website:

https://ir.wavelifesciences.com/events-publications/events. 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. 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 Wave Life Sciences

Wave Life Sciences (Nasdaq: WVE) is a biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health. Wave's RNA medicines platform, PRISM ®, combines multiple modalities, chemistry innovation and deep insights in human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Its toolkit of RNA-targeting modalities includes editing, splicing, RNA interference and antisense silencing, providing Wave with unmatched capabilities for designing and sustainably delivering candidates that optimally address disease biology. Wave's diversified pipeline includes clinical programs in Duchenne muscular dystrophy, Alpha-1 antitrypsin deficiency and Huntington's disease, as well as a preclinical program in obesity. Driven by the calling to "Reimagine Possible", Wave is leading the charge toward a world in which human potential is no longer hindered by the burden of disease. Wave is headquartered in Cambridge, MA. For more information on Wave's science, pipeline and people, please visit www.wavelifesciences.com and follow Wave on X (formerly Twitter) and LinkedIn.

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 and reporting of data and completion of our clinical trials, including interactions with regulators and any potential registration based on these data, and the timing and announcement of such events; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; our expectations with respect to how our clinical data successes to date may predict success for our future therapeutic candidates, future clinical data readouts and further validate of our platform; ongoing and future preclinical activities and programs; regulatory submissions and timing for regulatory feedback; the progress and potential benefits of our collaborations; the potential achievement of milestones under our collaborations and receipt of cash payments therefor; 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 benefits of our therapeutic candidates and pipeline compared to our competitors; patient population estimates related to our therapeutic candidates; our ability to design compounds using various modalities and the anticipated benefits of that approach; the breadth and versatility of our PRISM drug discovery and development platform; the expected benefits of our stereopure oligonucleotides compared with stereorandom oligonucleotides; the potential benefits of our RNA editing capability, including our AIMers, compared to others; the potential for certain of our programs to be best-in-class or first-in-class; the potential benefits of WVE-007, and the potential areas where we may be able to address obesity with WVE-007; the potential benefits that our "edit-verse" may provide us, including identifying new RNA editing targets; the status and progress of our programs relative to potential competitors; anticipated benefits of our proprietary manufacturing processes and our internal manufacturing capabilities; the benefits of RNA medicines generally; the strength of our intellectual property and the data that support our IP; the anticipated duration of our cash runway and our ability to fund future operations; our intended uses of capital; and our expectations regarding the impact of any potential global macro events 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 our product candidates; actions of regulatory authorities and their receptiveness to our adaptive trial designs and accelerated approval pathways, 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; the effectiveness of our RNA editing 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 the indications we are pursuing; our ability to maintain the company infrastructure and personnel needed to achieve our goals; and 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, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 153,958	$ 200,351
Accounts receivable	1,290	21,086
Prepaid expenses	12,147	9,912
Other current assets	4,680	4,024
Total current assets	172,075	235,373
Long-term assets:		
Property and equipment, net of accumulated depreciation of $44,459 and $42,709 as of June 30, 2024 and December 31, 2023, respectively	11,783	13,084
Operating lease right-of-use assets	20,329	22,637
Restricted cash	3,731	3,699
Other assets	900	156
Total long-term assets	36,743	39,576
Total assets	$ 208,818	$ 274,949
Liabilities, Series A preferred shares, and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 18,149	$ 12,839

Accrued expenses and other current liabilities	10,677	16,828
Current portion of deferred revenue	137,138	150,059
Current portion of operating lease liability	7,164	6,714
Total current liabilities	173,128	186,440
Long-term liabilities:		
Deferred revenue, net of current portion	9,582	15,601
Operating lease liability, net of current portion	21,711	25,404
Total long-term liabilities	31,293	41,005
Total liabilities	$ 204,421	$ 227,445
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at June 30, 2024 and December 31, 2023	$ 7,874	$ 7,874
Shareholders' equity (deficit):		
Ordinary shares, no par value; 122,479,289 and 119,162,234 shares issued and outstanding at June 30, 2024 and December 31, 2023, respectively	$ 950,530	$ 935,367
Additional paid-in capital	135,603	129,237
Accumulated other comprehensive loss	(279)	(124)
Accumulated deficit	(1,089,331)	(1,024,850)
Total shareholders' equity (deficit)	$ (3,477)	$ 39,630
Total liabilities, Series A preferred shares, and shareholders' equity (deficit)	$ 208,818	$ 274,949

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,	
	2024	2023	2024	2023
Revenue	$ 19,692	$ 22,106	$ 32,230	$ 35,035
Operating expenses:				
Research and development	40,393	33,314	73,840	64,293
General and administrative	14,296	12,265	27,845	24,500
Total operating expenses	54,689	45,579	101,685	88,793
Loss from operations	(34,997)	(23,473)	(69,455)	(53,758)
Other income, net:				
Dividend income and interest income	2,092	2,251	4,627	4,124
Other income (expense), net	(18)	118	347	1,125
Total other income, net	2,074	2,369	4,974	5,249
Loss before income taxes	(32,923)	(21,104)	(64,481)	(48,509)
Income tax benefit (provision)	—	—	—	—
Net loss	$ (32,923)	$ (21,104)	$ (64,481)	$ (48,509)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.25)	$ (0.20)	$ (0.50)	$ (0.47)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	129,527,003	105,462,414	129,399,340	103,768,971
Other comprehensive loss:				
Net loss	$ (32,923)	$ (21,104)	$ (64,481)	$ (48,509)
Foreign currency translation	(81)	(100)	(155)	(121)
Comprehensive loss	$ (33,004)	$ (21,204)	$ (64,636)	$ (48,630)

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Source: Wave Life Sciences USA, Inc.