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

November 12, 2024

Achieved first-ever RNA editing in humans in RestorAATion-2 trial of WVE-006 (GalNAc-AIMer) in alpha-1 antitrypsin deficiency and announced three wholly owned GalNAc-AIMer preclinical programs that offer first-in-class approaches to address unmet needs in cardiometabolic diseases

WVE-007 (INHBE GalNAc-siRNA) clinical trial on track for 1Q 2025; preclinical data demonstrates opportunities for monotherapy, for synergistic use with GLP-1s, and for maintenance to avoid rebound weight gain following cessation of GLP-1s

Received supportive initial feedback from FDA on WVE-003; FDA is engaged in discussing pathways to accelerated approval and open to Wave's plan to evaluate biomarkers, including caudate atrophy, as an endpoint to evaluate HD progression; IND submission expected in 2H 2025

Delivered positive interim data from FORWARD-53 study of WVE-N531; expect feedback on a pathway to accelerated approval from regulators, as well as the complete 48-week FORWARD-53 data, in 1Q 2025

Cash and cash equivalents of $310.9 million as of September 30, 2024, plus additional ~$28 million net proceeds received on October 1 from full exercise of greenshoe option, with runway expected into 2027

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

CAMBRIDGE, Mass., Nov. 12, 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 third quarter ended September 30, 2024, and provided a business update.

"Since the start of the third quarter, we have delivered positive clinical updates across DMD and AATD, unlocked RNA editing for Wave, and advanced our novel, wholly owned pipeline focused on GalNAc-conjugated programs," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Our achievement of proof-of-mechanism for WVE-006 marked a historic breakthrough for the oligonucleotide field with the first-ever in-human evidence of RNA editing, providing a strong foundation to expand our wholly owned editing pipeline. We are also advancing WVE-007 for obesity and WVE-N531 for DMD towards key milestones in the first quarter. In HD, we are encouraged by a potential path forward to bring the first-ever therapeutic approach that preserves healthy wild-type protein to people living with HD, a devastating disease with limited treatment options. We continue to receive substantial interest on HD, including from potential strategic partners. With the continued demonstration of our novel chemistry in the clinic and cash runway expected into 2027, we are well capitalized and well positioned to deliver multiple value inflection points across our portfolio as we continue to build a leading RNA medicines company."

Recent Business Highlights

GalNAc-RNA editing
AATD

- **WVE-006** is a GalNAc-conjugated, subcutaneously delivered, A-to-I RNA editing oligonucleotide (AIMer) that is uniquely designed to address Alpha-1 antitrypsin deficiency (AATD)-related lung disease, liver disease, or both. WVE-006 does not use a lipid-nanoparticle (LNP) delivery system.
- 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 worldwide sales in 2023). There are no approved therapies to address AATD liver disease, which ultimately requires many patients to undergo liver transplantation.
- WVE-006 is currently being evaluated in the top dose cohort of RestorAATion-1 (healthy volunteers) and in the first dose cohort of RestorAATion-2 in Pi*ZZ patients with AATD.
- In October, Wave announced positive proof-of-mechanism data from the first single dose cohort with the first two patients to reach day 57 in the ongoing RestorAATion-2 study, representing the first-ever clinical demonstration of RNA editing in humans. Circulating wild-type M-AAT protein in plasma reached a mean of 6.9 micromolar at day 15, representing more than 60% of total AAT. Mean total AAT protein increased from below the level of quantification at baseline to 10.8 micromolar at day 15, meeting the level that has been the basis for regulatory approval for AAT augmentation therapies. Increases in neutrophil elastase inhibition from baseline were consistent with production of functional M-AAT. WVE-006 was well-tolerated with a favorable safety profile across both RestorAATion-1 and RestorAATion-2.
- **Expected upcoming milestone:** Wave expects to share multidose data from RestorAATion-2 in 2025.

New AIMers

- At Research Day in October, Wave announced three new, wholly owned RNA editing programs that build on its recent achievement of the first-ever therapeutic RNA editing with WVE-006 in AATD. As with WVE-006, these programs leverage GalNAc conjugation and have efficient clinical paths to proof-of-concept. These new programs include PNPLA3, which aims to use an mRNA correction treatment approach for those at high risk for a variety of liver diseases, and LDLR and APOB which utilize first-in-class mRNA upregulation and mRNA correction treatment approaches (respectively) to achieve target LDL-c levels in heterozygous familial hypercholesterolemia patients.
- **Expected upcoming milestone:** Wave expects to select clinical candidates for PNPLA3, LDLR and APOB in 2025.

Obesity (GalNAc-siRNA)

- **WVE-007** is a GalNAc-conjugated small interfering RNA (GalNAc-siRNA) that targets INHBE as a novel approach to treat obesity. The approach is based on human genetics, where individuals who have a protective loss-of-function mutation in the INHBE gene have a healthier cardiometabolic profile, including less unhealthy visceral fat, lower triglycerides, and lower risk of type 2 diabetes and cardiovascular disease.
- At its recent Research Day, Wave shared data supporting WVE-007's potential to address obesity as a monotherapy, as an add-on to GLP-1s for further improvement of weight loss or to reduce the doses of GLP-1s, and for maintenance to prevent weight regain and weight cycling after discontinuing GLP-1s.
- **Expected upcoming milestone:** Wave expects to initiate a clinical trial for WVE-007 in the first quarter of 2025.

HD (allele-selective silencing)

- **WVE-003** is a first-in-class, allele-selective oligonucleotide for the treatment of Huntington's disease (HD). Results of the SELECT-HD clinical trial demonstrated the first-ever allele-selective reductions in CSF mutant huntingtin (mHTT) protein and preservation of healthy, wild-type huntingtin (wtHTT) protein with multiple doses of WVE-003, as well as a statistically significant correlation between mHTT reductions and slowing of caudate atrophy. By sparing wtHTT protein, which is critical to the health of the central nervous system, 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 (potential $5 billion commercial opportunity), and up to 80% of patients with HD may be addressed in the future with other SNP-targeted candidates (potential $10 billion commercial opportunity).
- At Wave's recent Research Day, Jeffrey Long, PhD, Professor of Psychiatry and Biostatistics at the University of Iowa, discussed the opportunity for caudate atrophy as a biomarker to expedite clinical development in HD. Dr. Long shared data which supports that the slowing of caudate atrophy predicts significant delays in the loss of function for people living with HD. The potential for changes in caudate volume to predict clinical outcomes in HD and its sensitivity to change early in the disease course makes it an optimal biomarker to enable smaller, more efficient clinical trials.
- In November 2024, Wave received supportive initial feedback from FDA, who recognize the severity of HD and are receptive to and engaged with Wave regarding a potential pathway to accelerated approval. FDA is open to Wave's plan to evaluate biomarkers, including caudate atrophy, as an endpoint to assess HD progression with the potential to predict clinical outcome. Planning is underway for a global, potentially registrational Phase 2/3 study of WVE-003, including finalization of key aspects of design.
- In November 2024, the FDA granted Orphan Drug Designation to WVE-003.
- **Expected upcoming milestone:** Wave expects to submit an Investigational New Drug ("IND") application for WVE-003 in the second half of 2025.

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 the third quarter, the FDA granted Rare Pediatric Disease Designation and Orphan Drug Designation to WVE-N531.
- In September, Wave announced positive interim data from the Phase 2 FORWARD-53 study of WVE-N531. The interim analysis was conducted after 24 weeks of 10 mg/kg dosing every two weeks. Dystrophin results, from a pre-specified analysis of ambulatory boys, showed mean absolute muscle content-adjusted dystrophin expression was 9.0% (range: 4.6-13.9%) as measured by Western Blot. The dystrophin expression was quantified from two isoforms consistent with those observed in Becker muscular dystrophy patients who display milder disease. 89% of ambulatory participants achieved muscle content-adjusted dystrophin levels of at least 5%. Mean exon skipping was 57% (range: 31-75%) as measured by RT-PCR.
- WVE-N531 could address up to 10% of the DMD population, which encompasses over 2,000 boys in the US and Europe. Wave is also advancing a broader DMD pipeline of oligonucleotides for skipping other exons, with the goal of providing new and best-in-class treatment options for up to 40% 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.
- **Expected upcoming milestone:** In the first quarter of 2025, Wave expects to deliver the complete 48-week FORWARD-53 data and receive feedback from regulators on a pathway to accelerated approval.

Financial Highlights

- Cash and cash equivalents were $310.9 million as of September 30, 2024, as compared to $200.4 million as of December 31, 2023. In the third quarter of 2024, Wave received approximately $187.5 million in net proceeds from the upsized September 2024 offering. Subsequent to the third quarter of 2024, on October 1, 2024, Wave received approximately $28.2 million in net proceeds from the September 2024 offering. Wave expects that its current cash and cash equivalents will be sufficient to fund operations into 2027. Potential future milestone and other payments to Wave under its GSK collaboration are not included in its cash runway.
- Revenue recognized was ($7.7) million for the third quarter of 2024, as compared to $49.2 million in the third quarter of 2023, which included one-time revenue recognition events under our Takeda Collaboration related to the termination of the C9 program and the achievement of a development milestone. The year over year decrease is primarily driven by these

one-time events in the prior year period. In addition, under our GSK collaboration, we recorded a non-cash reduction to cumulative revenue in the current period due to a change in the estimate to fulfill the performance obligations in accordance with revenue recognition standards. This adjustment changes the timing of revenue reporting for this program, with no impact on the program's progress or cash flow.

- Research and development expenses were $41.2 million in the third quarter of 2024, as compared to $31.6 million in the third quarter of 2023. General and administrative expenses were $15.0 million in the third quarter of 2024, as compared to $13.1 million in the third quarter of 2023.
- Net loss was $61.8 million for the third quarter of 2024, as compared to net income of $7.3 million for the third 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 third 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, and their potential to transition into clinical-stage programs ; the potential of our preclinical data to predict the behavior of our compounds in humans; 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 commercial opportunities that our therapeutic candidates may address; 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 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)

	September 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 310,948	$ 200,351
Accounts receivable	—	21,086
Prepaid expenses	10,572	9,912
Other current assets	2,995	4,024

Total current assets	324,515	235,373
Long-term assets:		
Property and equipment, net of accumulated depreciation of $45,490 and $42,709 as of September 30, 2024 and December 31, 2023, respectively	10,928	13,084
Operating lease right-of-use assets	19,119	22,637
Restricted cash	3,746	3,699
Other assets	196	156
Total long-term assets	33,989	39,576
Total assets	$ 358,504	$ 274,949
Liabilities, Series A preferred shares, and shareholders' equity		
Current liabilities:		
Accounts payable	$ 12,781	$ 12,839
Accrued expenses and other current liabilities	14,642	16,828
Current portion of deferred revenue	135,907	150,059
Current portion of operating lease liability	7,398	6,714
Total current liabilities	170,728	186,440
Long-term liabilities:		
Deferred revenue, net of current portion	18,490	15,601
Operating lease liability, net of current portion	19,772	25,404
Total long-term liabilities	38,262	41,005
Total liabilities	$ 208,990	$ 227,445
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at September 30, 2024 and December 31, 2023	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 148,392,939 and 119,162,234 shares issued and outstanding at September 30, 2024 and December 31, 2023, respectively	$ 1,139,714	$ 935,367
Additional paid-in capital	153,196	129,237
Accumulated other comprehensive loss	(159)	(124)
Accumulated deficit	(1,151,111)	(1,024,850)
Total shareholders' equity	$ 141,640	$ 39,630
Total liabilities, Series A preferred shares, and shareholders' equity	$ 358,504	$ 274,949

WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)

(In thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**
Revenue	$ (7,676)	$ 49,214	$ 24,554	$ 84,249
Operating expenses:				
Research and development	41,197	31,642	115,037	95,935
General and administrative	15,042	13,128	42,887	37,628
Total operating expenses	56,239	44,770	157,924	133,563
Income (loss) from operations	(63,915)	4,444	(133,370)	(49,314)
Other income, net:				
Dividend income and interest income	1,798	1,960	6,425	6,084
Other income, net	337	171	684	1,296
Total other income, net	2,135	2,131	7,109	7,380
Income (loss) before income taxes	(61,780)	6,575	(126,261)	(41,934)
Income tax benefit (provision)	—	677	—	677
Net income (loss)	$ (61,780)	$ 7,252	$ (126,261)	$ (41,257)
Less: net income attributable to participating securities	$ —	$ (257)	$ —	$ —
Net income (loss) attributable to ordinary shareholders, basic and diluted	$ (61,780)	$ 6,995	$ (126,261)	$ (41,257)
Net income (loss) per share attributable to ordinary shareholders—basic	$ (0.47)	$ 0.07	$ (0.97)	$ (0.39)
Weighted-average ordinary shares used in computing net income (loss) per share attributable to ordinary shareholders—basic	132,563,467	106,025,063	130,470,603	104,529,266
Net income (loss) per share attributable to ordinary shareholders—diluted	$ (0.47)	$ 0.07	$ (0.97)	$ (0.39)
Weighted-average ordinary shares used in computing net income (loss) per share attributable to ordinary shareholders—diluted	132,563,467	106,975,231	130,470,603	104,529,266

Other comprehensive income (loss):				
Net income (loss)	$ (61,780)	$ 7,252	$ (126,261)	$ (41,257)
Foreign currency translation	120	(32)	(35)	(153)
Comprehensive income (loss)	$ (61,660)	$ 7,220	$ (126,296)	$ (41,410)

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Source: Wave Life Sciences USA, Inc.