Wave Life Sciences Reports First Quarter 2025 Financial Results and Provides Business Update

May 8, 2025

Dosing complete in the first two cohorts of INLIGHT trial in obesity of WVE-007 (INHBE siRNA), designed to induce healthy weight loss by reducing fat without impacting muscle; clinical data on track for 2H 2025

Dosing underway in second single dose cohort (400 mg) and multidosing (200 mg) ongoing in RestorAATion-2 clinical trial of WVE-006 in individuals with PiZZ AATD; data from the complete 200 mg multidose and single dose cohorts expected in 3Q 2025; data from complete 400 mg single dose cohort expected in the fall of 2025

Delivered positive data from FORWARD-53 clinical trial of WVE-N531 in exon 53 amenable DMD including statistically significant and clinically meaningful improvement in TTR, substantial improvements in muscle health; NDA submission for accelerated approval with monthly dosing planned for 2026

IND submission expected 2H 2025 for potentially registrational WVE-003 Phase 2/3 study in HD with caudate atrophy as a primary endpoint

Cash and cash equivalents of $243.1 million as of March 31, 2025, with runway expected into 2027

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

CAMBRIDGE, Mass., May 08, 2025 (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 first quarter ended March 31, 2025, and provided a business update.

"We've continued our consistent execution across modalities as we completed dosing in the first two cohorts of our INLIGHT trial in obesity, advanced our RestorAATion-2 trial in AATD, and delivered positive data from our FORWARD-53 clinical trial in DMD. We are on track to deliver multiple clinical datasets this year that will further demonstrate our broad capabilities across modalities and our leadership in RNA medicines," said Paul Bolno, MD, MBA, President and Chief Executive Officer at Wave Life Sciences. "Our RestorAATion-2 trial of WVE-006, a subcutaneously-dosed GalNAc-conjugated RNA editing oligonucleotide, continues to advance and we are on track to deliver data from multiple dose cohorts this year, which will inform the therapeutic potential of WVE-006 and our pipeline of wholly-owned GalNAc-RNA editing programs. In obesity, we are evaluating WVE-007, our INHBE GalNAc-siRNA in our ongoing INLIGHT clinical trial, and are on track to deliver the first clinical data in the second half of this year. This program has potential to transform the obesity treatment paradigm with healthy weight loss, preservation of muscle mass, and infrequent dosing of once or twice a year."

Dr. Bolno continued, "In DMD, we delivered the first-ever substantial improvements in muscle health with an exon skipping therapy and showed statistically significant and clinically meaningful functional data from our FORWARD-53 trial of WVE-N531 in March. We have been engaged with the community in discussing our recent clinical results and are excited by the potential to bring a meaningful new potential treatment option to boys with DMD. In HD, our WVE-003 program has industry-leading CSF mutant lowering, and remains the only program to have successfully demonstrated allele-selective knockdown with wild-type HTT preservation in the clinic. We are actively engaged with both the HD community and prospective strategic partners, as we continue to prepare for our potentially registrational Phase 2/3 study."

Recent Business Highlights and Expected Milestones

Obesity

- **WVE-007** is a GalNAc-conjugated small interfering RNA (GalNAc-siRNA) designed to silence INHBE mRNA, an obesity target with strong evidence from human genetics. WVE-007 is Wave's first siRNA candidate to enter clinical development and uses Wave's best-in-class proprietary oligonucleotide chemistry.
- **INLIGHT** is an ongoing, first-in-human, placebo-controlled, clinical trial evaluating WVE-007 in adults living with overweight or obesity and assesses safety, tolerability, pharmacokinetics, biomarkers for target engagement, body weight and composition, and metabolic health.
- Today, Wave announced that it has completed dosing in the first and second single dose cohorts of INLIGHT.
- Next week, in oral presentations at the 32nd European Congress on Obesity (ECO) and the American Society of Gene and Cell Therapies (ASGCT) 28th Annual Meeting, Wave will highlight its preclinical data supporting WVE-007's potential in multiple treatment settings with potential for dosing once or twice a year, including:
    - A single dose of Wave's INHBE siRNA led to weight loss on par with semaglutide, but with no muscle loss.
    - When administered as an add-on to semaglutide, a single dose of Wave's INHBE siRNA doubled the amount of weight loss.
    - Wave's INHBE siRNA curtailed rebound weight gain when semaglutide treatment was discontinued, highlighting its potential as an off-ramp and maintenance treatment following GLP-1 treatment.
- **Expected milestones:** Wave expects to deliver clinical data from INLIGHT in the second half of 2025, including safety, tolerability and biomarkers reflective of healthy weight loss.

AATD (Alpha-1 antitrypsin deficiency)

- **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.
- **RestorAATion clinical program:** Multi-dosing is complete in RestorAATion-1 (healthy volunteers) at a dose level greater than those planned for any cohort in its ongoing RestorAATion-2 study. RestorAATion-2 is a Phase 1b/2a open-label study with both single and multiple ascending dose portions, which is evaluating the safety, tolerability, pharmacodynamics and pharmacokinetics of WVE-006 in individuals with AATD who have the homozygous Pi*ZZ mutation.
- Multi-dosing is ongoing in the first cohort of RestorAATion-2, where patients are receiving 200 mg subcutaneous doses every two weeks.
- Dosing is also underway in the second single dose cohort at 400 mg.

- In October 2024, Wave delivered proof-of-mechanism data from a single, lowest dose of WVE-006 from the first two patients in the ongoing RestorAATion-2 clinical 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, representing more than 60% of total AAT. Mean total AAT protein increased to 10.8 micromolar, meeting the level that has been the basis for regulatory approval for AAT augmentation therapies.
- **Expected milestones:** Wave expects to share data from the complete 200 mg multidose and single dose cohorts of RestorAATion-2 in the third quarter of 2025, and data from the complete 400 mg single dose cohort in the fall of 2025.

Emerging wholly owned siRNA and RNA editing pipeline

- Wave is advancing new targets across multiple disease areas to expand its pipeline of wholly owned programs in both rare and common diseases. Wave's pipeline of preclinical candidates utilize Wave's proprietary chemistry to achieve best-in-class silencing using siRNA and RNA editing in a variety of hepatic and extrahepatic tissues, including in the CNS with multiple AIMers such as MECP2. Within RNA editing, Wave has demonstrated the ability to correct single variants to restore wild-type protein function and to increase the stability of the mRNA transcript to upregulate protein levels.
- Wave's wholly owned RNA editing pipeline includes programs that use GalNAc conjugation and have efficient clinical paths to proof-of-concept. These include PNPLA3 mRNA correction to potentially address the nine million homozygous I148M carriers in the US and Europe at risk for a variety of liver diseases, and mRNA upregulation (LDLR) and mRNA correction (APOB), which together would address approximately one million people living with heterozygous familial hypercholesterolemia (HeFH) in the US and Europe.
- Next week, in an oral presentation at the ASGCT 28th Annual Meeting, Wave plans to share preclinical data demonstrating proof-of-principle for the use of AIMers in lung indications, including cystic fibrosis (CF). Available therapies for CF cannot address stop codon mutations in the CFTR gene. In human bronchial epithelial cells with CFTR mutation W1282X, CFTR AIMers increased expression of CFTR mRNA 3-fold and restored up to 50% of functional wild-type CFTR protein levels.
- **Expected milestones:** Wave plans to share new preclinical data from hepatic and extra-hepatic RNA editing programs in 2025 and to initiate clinical development of additional RNA editing programs, including PNPLA3, LDLR, and APOB, in 2026.

DMD (Duchenne muscular dystrophy)

- **WVE-N531** is an exon skipping oligonucleotide being developed as a disease modifying treatment for boys with Duchenne muscular dystrophy amenable to exon 53 skipping. WVE-N531 was designed using Wave's best-in-class oligonucleotide chemistry modifications, including PN backbone chemistry. WVE-N531 has received Orphan Drug Designation and Rare Pediatric Disease Designation from the U.S. Food & Drug Administration.
- In March 2025, Wave announced positive 48-week data from its Phase 2, open-label FORWARD-53 clinical trial of WVE-N531, which included:
    - Statistically significant and clinically meaningful improvement of 3.8 seconds in Time-to-Rise vs. natural history with largest effect observed relative to any approved dystrophin restoration therapy at 48 weeks; additional functional benefits observed in other outcome measures including NSAA.
    - First-ever demonstration of substantial improvements in muscle health with exon skipping – statistically significant reduction in fibrosis driven by decreases in inflammation and necrosis, coupled with transition from regenerative to mature muscle; decreases in creatine kinase and circulating inflammatory biomarkers.
    - Dystrophin expression stabilized between 24 and 48 weeks and averaged 7.8%, with 88% of boys above 5% average dystrophin.
    - WVE-N531 remains safe and well-tolerated with no Serious Adverse Events.
- All participants in FORWARD-53 elected to advance to the extension portion of the clinical trial, which is currently ongoing with boys receiving monthly doses of WVE-N531. To augment monthly data and ensure a monthly regimen at a potential launch, Wave is also expanding FORWARD-53 to include additional boys who will be dosed monthly.
- Also in March 2025, Wave announced that the company met with the U.S. Food and Drug Administration (FDA) on WVE-N531 to discuss its interim 24-week data and initial plans for the confirmatory trial, where the Agency confirmed that the accelerated approval pathway using dystrophin expression as a surrogate endpoint remains open.
- **Expected milestones:** Wave plans to file a New Drug Application (NDA) in 2026 to support accelerated approval of WVE-N531 with monthly dosing. Wave expects to submit clinical trial applications (CTAs) for additional exon skipping programs in 2026.

HD (Huntington's disease)

- **WVE-003** is a first-in-class, allele-selective oligonucleotide for the treatment of Huntington's disease (HD). In the SELECT-HD clinical trial, data demonstrated the first-ever allele-selective reduction in CSF mHTT protein and preservation of healthy, wtHTT with multiple doses of WVE-003, as well as a statistically significant correlation between mHTT reduction and slowing of caudate atrophy. By reducing mHTT at the mRNA and protein level, WVE-003 addresses underlying drivers of neurodegeneration. In addition, 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.
- Wave has 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. Preparation is ongoing for a potentially registrational, global Phase 2/3 study of WVE-003 in adults with SNP3 and HD using caudate atrophy as a primary endpoint.
- **Expected milestones:** Wave expects to submit an Investigational New Drug (IND) application for a potentially registrational Phase 2/3 study of WVE-003 in HD in the second half of 2025.

Financial Highlights

- Cash and cash equivalents were $243.1 million as of March 31, 2025, compared to $302.1 million as of December 31, 2024. Wave expects that its current cash and cash equivalents will be sufficient to fund operations into 2027. Potential future milestones and other payments to Wave under its GSK collaboration are not included in its cash runway.
- Revenue recognized was $9.2 million for the first quarter of 2025 as compared to $12.5 million in the prior year quarter.
- Research and development expenses were $40.6 million in the first quarter of 2025 as compared to $33.4 million in the same period in 2024.
- General and administrative expenses were $18.4 million in the first quarter 2025 as compared to $13.5 million in the same period in 2024.
- Net loss was $46.9 million for the first quarter of 2025 as compared to $31.6 million in the prior year quarter.

Investor Conference Call and Webcast
Wave will host an investor conference call today at 8:30 a.m. ET to review the first quarter 2025 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 by dialing (833) 630-1956 (domestic) or (412) 317-1837 (international). 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 common 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 Alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy, Huntington's disease, and Obesity, as well as several preclinical programs utilizing the company's broad RNA therapeutics toolkit. 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, endpoints, dose levels and dosing frequency for our investigational therapeutics in 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 and data readouts and may further validate our platform; 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 submission of marketing approval applications to regulators, approval thereof, and the potential commercialization of our late-stage programs; the progress and potential benefits of collaborations and strategic partnerships; the potential achievement of milestones under any collaborations; our identification of future product candidates and their therapeutic potential; the anticipated benefits of our therapeutic candidates and pipeline compared to our competitors; the potential unmet medical needs and addressable patient population estimates related to our therapeutic candidates; our ability to design compounds using the most appropriate of our multiple modalities and the anticipated benefits of that approach; the breadth and versatility of our 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 or to change the existing treatment paradigm or show substantial benefits over existing standards of care; 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 trial designs and accelerated approval pathways, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing interactions with regulatory authorities; the effectiveness of our drug discovery and development platform; 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.

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WAVE LIFE SCIENCES LTD.
UNAUDITED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	March 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 243,075	$ 302,078
Accounts receivable	—	1,422
Prepaid expenses	8,062	9,544
Other current assets	6,839	7,350
Total current assets	257,976	320,394
Long-term assets:		
Property and equipment, net of accumulated depreciation of $47,027 and $46,329 as of March 31, 2025 and December 31, 2024, respectively	9,566	10,128
Operating lease right-of-use assets	16,581	17,870

Restricted cash	3,772	3,760
Other assets	448	55
Total long-term assets	30,367	31,813
Total assets	$ 288,343	$ 352,207
Liabilities, Series A preferred shares, and shareholders' equity		
Current liabilities:		
Accounts payable	$ 14,358	$ 16,262
Accrued expenses and other current liabilities	7,813	21,081
Current portion of deferred revenue	57,312	65,972
Current portion of operating lease liability	7,884	7,638
Total current liabilities	87,367	110,953
Long-term liabilities:		
Deferred revenue, net of current portion	5,584	6,099
Operating lease liability, net of current portion	15,715	17,766
Total long-term liabilities	21,299	23,865
Total liabilities	$ 108,666	$ 134,818
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at March 31, 2025 and December 31, 2024	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 154,093,313 and 153,037,286 shares issued and outstanding at March 31, 2025 and December 31, 2024, respectively	$ 1,179,336	$ 1,175,181
Additional paid-in capital	161,407	156,454
Accumulated other comprehensive loss	(204)	(262)
Accumulated deficit	(1,168,736)	(1,121,858)
Total shareholders' equity	$ 171,803	$ 209,515
Total liabilities, Series A preferred shares, and shareholders' equity	$ 288,343	$ 352,207

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

(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2025	**2024**
Revenue	$ 9,175	$ 12,538
Operating expenses:		
Research and development	40,622	33,447
General and administrative	18,357	13,549
Total operating expenses	58,979	46,996
Loss from operations	(49,804)	(34,458)
Other income, net:		
Interest income	2,875	2,535
Other income, net	51	365
Total other income, net	2,926	2,900
Loss before income taxes	(46,878)	(31,558)
Income tax benefit (provision)	—	—
Net loss	$ (46,878)	$ (31,558)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.29)	$ (0.24)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	162,527,026	129,271,678
Other comprehensive loss:		
Net loss	$ (46,878)	$ (31,558)
Foreign currency translation	58	(74)
Comprehensive loss	$ (46,820)	$ (31,632)



Source: Wave Life Sciences USA, Inc.