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

May 9, 2024

RestorAATion-2 clinical trial of WVE-006 in AATD patients underway; expected proof-of-mechanism data in patients with AATD remains on track for 2024

INHBE program for obesity expected clinical trial initiation in 1Q 2025; preclinical data demonstrate weight loss similar to semaglutide, fat loss with no loss of muscle mass, and curtailed rebound weight gain upon cessation of semaglutide, with potential for dosing 1 – 2 times per year

Continued momentum in GSK collaboration; advancing first two GSK collaboration programs following successful target validation; both programs utilize Wave's GalNAc-siRNA format and discovery collaboration continues to span all Wave modalities, including RNA editing

Clinical data on track for first-in-class, allele-selective HD program (expected 2Q 2024) and potentially registrational FORWARD-53 trial in DMD (expected 3Q 2024)

Cash and cash equivalents of $181 million as of March 31, 2024; with an additional $12 million aggregate initiation payment earned under GSK collaboration subsequent to quarter-end for advancement of programs; runway expected into 4Q 2025

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

CAMBRIDGE, Mass., May 09, 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 first quarter ended March 31, 2024, and provided a business update.

"Since our last update, we have made excellent progress across our multimodal pipeline of novel RNA medicines and continued to advance our collaboration with GSK. We are on-track to deliver key data sets this year, which enable opportunities to unlock the broad potential of our RNA editing, silencing and splicing capabilities," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "In RNA editing, we are advancing WVE-006, having used data from healthy volunteers in RestorAATion-1 to identify a starting dose in our RestorAATion-2 study that is expected to engage target in patients. With RestorAATion-2 now underway, we remain on track to deliver expected proof of mechanism data in patients with AATD this year, which would represent the first-ever clinical demonstration of RNA editing and be an important milestone for the alpha-1 community, as well as serve to validate our wholly owned RNA editing pipeline."

Dr. Bolno continued, "In addition to pioneering the field of RNA editing, we are working expeditiously to advance our GalNAc-siRNA INHBE program in obesity and expect to initiate a clinical trial in the first quarter of next year. In DMD and HD, we are approaching clinical data readouts as we plan to deliver multidose data for our allele-selective HD program in the second quarter and potentially registrational data from our FORWARD-53 trial in DMD in the third quarter. Our efforts to accelerate development of our INHBE program and advance our pipeline and collaborations have laid a strong foundation for Wave's future and we look forward to demonstrating our leadership in RNA medicines as we reimagine what's possible for science, for medicine, and for human health."

Recent Business Highlights

AATD and AIMer pipeline (RNA editing)

- **RestorAATion-2 underway; clinical program investigating WVE-006 as a first- and best-in-class treatment for alpha-1 antitrypsin deficiency (AATD)**
  - WVE-006 is Wave's GalNAc-conjugated, subcutaneously delivered, RNA editing oligonucleotide 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.
  - The RestorAATion-2 clinical trial is now underway. RestorAATion-2 is a Phase 1b/2a open label study designed to evaluate the safety, tolerability, pharmacodynamics (PD) and pharmacokinetics (PK) of WVE-006 in patients with AATD who have the homozygous Pi*ZZ mutation. The trial includes both single ascending dose (SAD) and multiple ascending dose (MAD) portions. It is designed to provide an efficient path to proof-of-mechanism as measured by restoration of wild-type alpha-1 antitrypsin (M-AAT) protein in serum.
  - Wave's progress in dose-escalating healthy volunteers in RestorAATion-1 enabled the quick identification of a starting dose level in RestorAATion-2 that, based on preclinical data, is expected to engage target in patients.
  - In addition to WVE-006, Wave continues to advance its pipeline of wholly owned RNA editing therapeutics across a range of high-impact GalNAc-hepatic and extra-hepatic targets. Powered by genetic datasets and deep learning models, Wave is 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. Wave plans to share new preclinical data from its wholly owned RNA editing pipeline in 2024.
  - **Expected upcoming milestone:** Wave expects to deliver proof-of-mechanism data from RestorAATion-2 in patients with AATD in 2024

Obesity (siRNA)

- **Advancing lead clinical candidate for INHBE program with a potentially best-in-class profile for obesity toward**

anticipated clinical trial initiation in 1Q 2025

- Wave's wholly owned INHBE clinical candidate is a GalNAc-small interfering RNA (siRNA) that utilizes Wave's next generation siRNA format and is designed to silence the INHBE (Inhibin βE) gene, with a goal of inducing lipolysis (fat-burning) while preserving muscle mass to restore and maintain a healthy metabolic profile.
- INHBE loss-of-function (LoF) heterozygous human carriers have a favorable cardiometabolic profile, including reduced abdominal obesity and reduced odds of type 2 diabetes and coronary artery disease. Silencing INHBE is expected to recapitulate the cardiometabolic profile of these LoF carriers and may also address limitations of GLP-1s.
- 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 preclinical mouse models. Data also demonstrated weight loss 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 an ongoing, head-to-head study in diet-induced obesity mice, Wave has observed a weight loss effect from a single dose of its INHBE GalNAc-siRNA similar to semaglutide. In addition, 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 its INHBE candidate in the first quarter of 2025.

GSK Collaboration

- **Advancing first two collaboration programs recently selected by GSK following target validation; programs utilize Wave's next generation GalNAc siRNA format**
  - In April 2024, GSK selected its first two Collaboration Programs, which are in hepatology, to advance to development candidates following achievement of target validation. GSK will provide an aggregate initiation payment of $12 million to Wave.
  - The first two GSK Collaboration Programs utilize Wave's GalNAc-siRNA formats. Under the agreement, GSK can advance up to eight programs leveraging Wave's PRISM platform and multiple RNA-targeting modalities, including RNA editing, with target validation ongoing in multiple therapy areas.
  - In total, Wave is eligible for up to $3.3 billion in potential milestone payments, as well as tiered royalties on net sales, for GSK's eight Collaboration Programs and WVE-006, for which GSK has an exclusive global license.

DMD (exon skipping)

- **Advancing FORWARD-53 clinical trial toward potentially registrational 24-week dystrophin data in the third quarter of 2024**
  - Wave's WVE-N531 program for boys with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping is designed to induce production of endogenous, functional dystrophin protein.
  - In Part A of Wave's WVE-N531 trial, WVE-N531 demonstrated industry-leading exon skipping levels of 53%, muscle tissue concentrations of 42 µg/g (~42,000 ng/g), and myogenic stem cell distribution in all study participants.
  - WVE-N531 is currently being evaluated in the ongoing FORWARD-53 clinical trial of 11 boys with DMD, which is powered to evaluate endogenous, functional dystrophin expression following 24 and 48 weeks of 10 mg/kg dosing administered every-other-week. The primary endpoint is dystrophin protein levels, and the trial will also evaluate pharmacokinetics, digital and functional endpoints, and safety and tolerability.
  - 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 treatment options for a larger population of boys with DMD.
  - **Expected upcoming milestone:** Wave expects to deliver data, including dystrophin protein expression from muscle biopsies at 24 weeks, in the third quarter of 2024.

HD (antisense silencing)

- **WVE-003 SELECT-HD multi-dose data with extended follow-up remains on track for 2Q 2024; first-in-class program designed to lower mutant HTT while sparing wild-type HTT**
  - WVE-003 is a first-in-class investigational allele-selective Huntington's disease (HD) therapeutic designed to reduce mutant huntingtin (mHTT) protein while also sparing healthy wild-type huntingtin (wtHTT) protein. Due to the significance of wtHTT function for the health of the central nervous system and the potential for mHTT to disrupt wtHTT function, selectively lowering mHTT while preserving wtHTT protein expression and function may offer advantages over nonselective HTT-lowering approaches for the treatment of HD.
  - WVE-003 has demonstrated single-dose reductions in mean mHTT in cerebrospinal fluid of 35% compared to placebo, with preservation of wtHTT, as previously shared in September 2022.
  - The ongoing multi-dose portion of the SELECT-HD clinical trial is evaluating a cohort of 24 patients with HD receiving 30 mg doses of WVE-003 administered every eight weeks.
  - Data from the ongoing SELECT-HD clinical trial will form the basis for decision making for Wave's advancement of this program, including supporting an opt-in package for Takeda.
  - **Expected upcoming milestone:** Wave expects to report data from the 30 mg multi-dose cohort with extended follow-up, along with all single-dose data, in the second quarter of 2024.

Corporate

- **Dr. Erik Ingelsson appointed CSO; builds on Wave's recent progress advancing innovative genetic targets and adds experience to accelerate rapid identification and translation of unique genetic insights**
  - Today, Wave announced the appointment of Erik Ingelsson, MD, PhD, as Chief Scientific Officer (CSO). Dr. Ingelsson joins Wave to drive the emerging therapeutic portfolio strategy, including growing its genetics and genomics capabilities for identifying new, high impact targets and leveraging Wave's multimodal platform to advance transformative RNA medicines. Dr. Ingelsson brings deep expertise in genetics and drug discovery, as well as substantial experience in metabolic diseases, such as obesity, MASH and cardiovascular disease.
  - Most recently, Dr. Ingelsson served as Senior Vice President, Head of Target Discovery, at GSK, and prior to that, was SVP of Genomic Sciences at GSK. Previously, he was a Professor of Medicine at Stanford University. (See May 9, 2024 press release here)

Financial Highlights

- Cash and cash equivalents were $180.9 million as of March 31, 2024, compared to $200.4 million as of December 31, 2023. Subsequent to March 31, 2024, GSK advanced two programs to candidate development, triggering a $12.0 million aggregate initiation payment to Wave. 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 $12.5 million for the first quarter of 2024, as compared to $12.9 million in the first quarter of 2023. The slight decrease in revenue was due to decreased revenue from the Takeda collaboration. Revenue from the GSK collaboration was consistent for the first quarter of 2024 and 2023.
- Research and development expenses were $33.4 million in the first quarter of 2024, as compared to $31.0 million in the first quarter of 2023. General and administrative expenses were $13.5 million in the first quarter of 2024, as compared to $12.2 million in the first quarter of 2023.
- Net loss was $31.6 million for the first quarter of 2024, as compared to $27.4 million for the first 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 first 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 announcement of such events; the protocol, design and endpoints of our clinical trials; the future performance and results of our programs in clinical trials; ongoing and future preclinical activities and programs; regulatory submissions; 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; 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 our GalNAc-conjugated siRNA program targeting INHBE; 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, 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)

	March 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 180,922	$ 200,351
Accounts receivable	—	21,086
Prepaid expenses	11,139	9,912
Other current assets	4,706	4,024
Total current assets	196,767	235,373
Long-term assets:		
Property and equipment, net of accumulated depreciation of $43,687 and $42,709 as of March 31, 2024 and December 31, 2023, respectively	12,418	13,084
Operating lease right-of-use assets	21,502	22,637
Restricted cash	3,715	3,699
Other assets	868	156
Total long-term assets	38,503	39,576
Total assets	$ 235,270	$ 274,949
Liabilities, Series A preferred shares, and shareholders' equity		
Current liabilities:		
Accounts payable	$ 11,730	$ 12,839
Accrued expenses and other current liabilities	6,621	16,828
Current portion of deferred revenue	140,586	150,059
Current portion of operating lease liability	6,936	6,714
Total current liabilities	165,873	186,440
Long-term liabilities:		
Deferred revenue, net of current portion	12,536	15,601
Operating lease liability, net of current portion	23,598	25,404
Total long-term liabilities	36,134	41,005
Total liabilities	$ 202,007	$ 227,445
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at March 31, 2024 and December 31, 2023	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 122,321,384 and 119,162,234 shares issued and outstanding at March 31, 2024 and December 31, 2023, respectively	$ 949,877	$ 935,367
Additional paid-in capital	132,118	129,237
Accumulated other comprehensive loss	(198)	(124)
Accumulated deficit	(1,056,408)	(1,024,850)
Total shareholders' equity	$ 25,389	$ 39,630
Total liabilities, Series A preferred shares, and shareholders' equity	$ 235,270	$ 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 March 31,	
	2024	2023
Revenue	$ 12,538	$ 12,929
Operating expenses:		
Research and development	33,447	30,979
General and administrative	13,549	12,235
Total operating expenses	46,996	43,214
Loss from operations	(34,458)	(30,285)
Other income, net:		
Dividend income and interest income	2,535	1,873
Other income, net	365	1,007
Total other income, net	2,900	2,880

Loss before income taxes	(31,558)	(27,405)
Income tax benefit (provision)	—	—
Net loss	$ (31,558)	$ (27,405)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.24)	$ (0.27)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	129,271,678	102,056,712
Other comprehensive loss:		
Net loss	$ (31,558)	$ (27,405)
Foreign currency translation	(74)	(21)
Comprehensive loss	$ (31,632)	$ (27,426)

Investor Contact:
Kate Rausch
+1 617-949-4827
krausch@wavelifesci.com

Media Contact:
Alicia Suter
+1 617-949-4817
asuter@wavelifesci.com

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