Omega Therapeutics Reports Fourth Quarter and Full Year 2023 Financial Results and Provides Strategic Update

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- *Advanced OTX-2002 in MYCHELANGELO™ I trial; initial cohorts demonstrated encouraging disease control rate in late-stage HCC patients*
- *Established a research collaboration with Novo Nordisk to develop an epigenomic controller for obesity, expanding the pipeline into the cardiometabolic space*
- *Announced strategic prioritization to focus resources on potential near-term value drivers, support long-term growth, and extend cash runway into Q1 2025*

CAMBRIDGE, Mass., March 28, 2024 (GLOBE NEWSWIRE) -- Omega Therapeutics, Inc. (Nasdaq: OMGA) ("Omega"), a clinical-stage biotechnology company pioneering the development of a new class of programmable epigenomic mRNA medicines, today announced financial results for the fourth quarter and full year ended December 31, 2023, and a strategic prioritization initiative to focus resources on near-term milestones to support long-term shareholder value.

"2023 was an important year for Omega where we executed to plan and demonstrated clinical validation of an epigenomic controller to regulate c-MYC in humans for the first time. These proof-of-platform clinical data, coupled with our research collaboration with Novo Nordisk in obesity, support the ability of the OMEGA platform to potentially address epigenomic regulation of almost all human genes across broad therapeutic areas including cancer, cardiometabolic conditions and liver regeneration," said Mahesh Karande, President and Chief Executive Officer of Omega Therapeutics. "Initial clinical data from our ongoing Phase 1/2 MYCHELANGELO I trial of OTX-2002 demonstrated controlled modulation of MYC expression levels, one of the most challenging gene targets in oncology, and an encouraging disease control rate and stable disease in heavily pre-treated, late-stage HCC patients. We are within what we believe is a clinically meaningful dose range and, as we continue to see a promising safety profile for OTX-2002, have recently opened enrollment of Cohort 5. We look forward to sharing additional updates from this program throughout 2024."

"Today we also announced a strategic prioritization, implemented to ensure we have sufficient resources to advance our lead program and maximize near- and long-term value creation from our platform. As part of this initiative, we are taking difficult but necessary actions to streamline our team and optimize our R&D efforts and cost structure to extend our cash runway into the first quarter of 2025. These changes will unfortunately affect a number of our colleagues, and we are grateful for their dedication and contributions to our mission," continued Mr. Karande. "As we sharpen our focus, we look forward to the opportunities ahead to generate meaningful clinical data for OTX-2002, continue to demonstrate the broad potential of our platform, and establish additional partnerships. We remain steadfast in our mission to pioneer a new class of programmable epigenomic mRNA medicines to transform the treatment of a broad range of diseases."

Recent Highlights and Key Anticipated Milestones

Development Pipeline and Platform

- **Advanced the Phase 1/2 MYCHELANGELO™ I clinical trial evaluating OTX-2002 in patients with hepatocellular carcinoma (HCC):**
  - OTX-2002 continues to advance in monotherapy dose escalation.
  - As of March 24, 2024, data from the first three cohorts (0.02 mg/kg – 0.06 mg/kg) showed:
    - OTX-2002 continued to be generally well tolerated, with no dose-limiting toxicities observed.
    - Consistent dose-dependent pharmacokinetics with no drug accumulation observed following repeat doses.
    - All patients demonstrated controlled modulation and downregulation of MYC mRNA expression, an important oncogene regulating cell function and cell death.
    - The interim disease control rate (DCR) for the target population of HCC patients was 80%, reflecting 4 out of 5 efficacy-evaluable patients having a best overall response of stable disease. These patients had an average of three or more previous therapies and entered the trial with a life expectancy of less than 12 weeks. The DCR for patients with non-HCC solid tumors in the trial (n=5) was 40%,

indicating the potential specificity of OTX-2002 for HCC.
    - The Company continues to evaluate patients with HCC in Cohort 4 at the 0.12 mg/kg dose level, which recently cleared the 28-day dose limiting toxicity (DLT) window. Based on preclinical experience and modeling, Omega believes this dose level is within the expected active dose range. In March 2024, the Company opened enrollment for Cohort 5 at a dose level of 0.3 mg/kg.
    - Omega expects to report additional updated clinical data from monotherapy dose escalation in mid-2024.
    - The Company plans for expansion into monotherapy and combination settings in mid-2024.

- **Announced research collaboration with Novo Nordisk to develop a novel therapeutic for obesity management:**
    - The collaboration will leverage Novo Nordisk's expertise in research and development within cardiometabolic diseases and Omega's proprietary platform technology to develop an epigenomic controller designed to enhance metabolic activity.
    - Unlike traditional approaches focused on appetite suppression, the program aims to leverage precision epigenomic control to enhance thermogenesis, a naturally occurring metabolic process that burns calories.
    - Under the terms of the agreement, Novo Nordisk will reimburse all R&D costs and has the right to select one target to advance for clinical development. Omega and Flagship's Pioneering Medicines are eligible to receive up to $532 million in upfront, development and commercial milestone payments, as well as tiered royalties on annual net sales of a licensed product, which will be split equally between the parties.
- **Continued to advance and expand OMEGA platform capabilities:**
    - Presented new preclinical data supporting the breadth of Omega's platform capabilities, including bidirectional and multiplexed epigenomic control of gene expression in liver inflammation and fibrosis at the American Association for the Study of Liver Diseases' (AASLD) The Liver Meeting® 2023.
        - A HNF4A-targeting epigenomic controller led to a durable increase in HNF4α expression, preferential upregulation of HNF4α P1 promoter isoforms, and reduced key measures of fibrosis both *in vitro* and *in vivo*, supporting this development candidate's potential for the treatment of fibrotic liver disease.
        - In preclinical models, liver-specific multiplexed targeting of CXCL9, CXCL10 and CXCL11 via an epigenomic controller led to a significant reduction in T-cell migration, a critical driver of inflammation-induced liver injury, supporting the potential of this approach as a novel treatment for inflammatory liver diseases.

Corporate

- **Announced cost reduction and strategic prioritization initiative to maximize near- and long-term value creation opportunities:**
    - Following a strategic review, the Company has focused its pipeline and reduced overall headcount by approximately 35%. These fiscally disciplined actions are expected to extend the Company's cash runway into Q1 2025.
    - Positions the Company to achieve key clinical data readouts from the monotherapy dose escalation and dose expansion stages of the MYCHELANGELO I clinical trial.
    - The Company will prioritize certain preclinical programs and platform efforts:
        - Prioritized preclinical programs include OTX-2101 for non-small cell lung cancer (NSCLC), the HNF4A program in liver regeneration, and development of an

epigenomic controller for obesity in collaboration with Novo Nordisk.
    - Core work on platform biology, epigenomic controllers, and characterization of LNP delivery to the lung and other tissues will continue.
- An updated corporate presentation is available on the Investors section of the Company's website at https://ir.omegatherapeutics.com/.

Fourth Quarter and Full Year 2023 Financial Results

As of December 31, 2023, the Company had cash, cash equivalents and marketable securities totaling $73.4 million, which is expected to fund operations into Q1 2025.

Research and development (R&D) expenses for the fourth quarter of 2023 were $15.5 million, compared to $26.0 million for the fourth quarter of 2022. R&D expenses for 2023 were $77.2 million compared to $81.2 million in 2022. The $4.0 million decrease in R&D expenses in 2023 compared to 2022 was primarily due to lower external research and manufacturing costs, consulting and professional fees, and lab expenses, partially offset by an increase in personnel-related expenses, including stock-based compensation to support business growth, and facilities and other costs.

General and administrative (G&A) expenses for the fourth quarter of 2023 were $6.2 million, compared to $5.7 million for the fourth quarter of 2022. G&A expenses for 2023 were $26.2 million, compared to $23.7 million in 2022. The $2.5 million increase in G&A expenses in 2023 compared to 2022 was primarily due to higher professional and consulting fees, and facilities and other administrative costs.

Net loss for the fourth quarter of 2023 was $20.2 million, compared to $30.8 million for the fourth quarter of 2022. Net loss for the year ended December 31, 2023, was $97.4 million, compared to a net loss of $102.7 million for the year ended December 31, 2022. The decrease in net loss for 2023 compared to 2022 was primarily due to decreases in R&D expenses.

About Omega Therapeutics

Omega Therapeutics is a clinical-stage biotechnology company pioneering the development of a new class of programmable epigenomic mRNA medicines to treat or cure a broad range of diseases. By pre-transcriptionally modulating gene expression, Omega's approach enables precision epigenomic control of nearly all human genes, including historically undruggable and difficult-to-treat targets, without altering native nucleic acid sequences. Founded in 2017 by Flagship Pioneering following breakthrough research by world-renowned experts in the field of epigenetics, Omega is led by a seasoned and accomplished leadership team with a track record of innovation and operational excellence. The Company is committed to revolutionizing genomic medicine and has a pipeline of therapeutic candidates derived from its OMEGA platform spanning oncology, regenerative medicine, and multigenic diseases including inflammatory and cardiometabolic conditions.

For more information, visit omegatherapeutics.com, or follow us on X and LinkedIn.

About the OMEGA Platform

The OMEGA platform leverages the Company's deep understanding of gene regulation, genomic architecture and epigenetic mechanisms to design programmable epigenomic mRNA medicines that precisely target and modulate gene expression at the pre-transcriptional level. Combining world-class data science capabilities with rational drug design and customized delivery, the OMEGA platform enables control of fundamental epigenetic processes and reprogramming of cellular physiology to address the root cause of disease. Omega's modular and programmable mRNA medicines, called epigenomic controllers, target specific genomic loci within insulated genomic domains with high specificity to durably tune single or multiple genes to treat and cure diseases through unprecedented precision epigenomic control.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the timing, progress and design of our ongoing Phase 1/2 MYCHELANGELO™ I clinical trial and our preclinical studies, as well as the timing of announcements of data related thereto; the potential of the OMEGA platform to engineer programmable epigenomic mRNA therapeutics that successfully regulate gene expression by targeting insulated genomic domains; expectations surrounding the potential of our product candidates, including OTX-2002 and OTX-2101; expectations regarding our pipeline, including trial design, initiation of preclinical studies and advancement of multiple preclinical development programs in oncology, immunology, regenerative medicine, and select monogenic diseases; potential franchise opportunities; our anticipated cash runway into the first quarter of 2025; our prioritization of certain preclinical programs and platform efforts; and our plans to ensure that we have sufficient resources to advance our lead program, support long term growth, and accomplish our mission. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the novel technology on which our product candidates are based makes it difficult to predict the time and cost of preclinical and clinical development and subsequently obtaining regulatory approval, if at all; the substantial development and regulatory risks associated with epigenomic controllers due to the novel and unprecedented nature of this new category of medicines; our limited operating history; the incurrence of significant losses and the fact that we expect to continue to incur significant additional losses for the foreseeable future; our need for substantial additional financing; our investments in research and development efforts that further enhance the OMEGA platform, and their impact on our results; uncertainty regarding preclinical development, especially for a new class of medicines such as epigenomic controllers; potential delays in and unforeseen costs arising from our clinical trials; the fact that our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their regulatory development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences; the impact of increased demand for the manufacture of mRNA and LNP based vaccines to treat COVID-19 on our development plans; difficulties manufacturing the novel technology on which our epigenomic controller candidates are based; our ability to adapt to rapid and significant technological change; our reliance on third parties for the manufacture of materials; our ability to successfully acquire and establish our own manufacturing facilities and infrastructure; our reliance on a limited number of suppliers for lipid excipients used in our product candidates; our ability to advance our product candidates to clinical development; and our ability to obtain, maintain, enforce and adequately protect our intellectual property rights. These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2023, and our other filings with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

Omega Therapeutics, Inc.
Consolidated statements of operations and comprehensive loss
(Unaudited, In thousands except share and per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
Collaboration revenue from related party	$ 989	$ 735	$ 3,094	$ 2,073
Operating expenses:				
Research and development	15,531	25,968	77,169	81,167
General and administrative	6,157	5,734	26,186	23,672
Total operating expenses	21,688	31,702	103,355	104,839
Loss from operations	(20,699)	(30,967)	(100,261)	(102,766)
Other income (expense), net:				
Interest income, net	487	248	2,810	222
Other income (expense), net	(2)	(107)	23	(157)
Total other income, net	485	141	2,833	65
Net loss	$ (20,214)	$ (30,826)	$ (97,428)	$ (102,701)
Net loss per common stock attributable to common stockholders, basic and diluted	$ (0.37)	$ (0.64)	$ (1.80)	$ (2.14)
Weighted-average common stock used in net loss per share attributable to common stockholders, basic and diluted	55,143,137	47,895,083	54,010,996	47,880,819
Comprehensive loss:				
Net loss	$ (20,214)	$ (30,826)	$ (97,428)	$ (102,701)
Other comprehensive income (loss):				
Unrealized gain (loss) on marketable securities	72	438	465	(417)
Comprehensive loss	$ (20,142)	$ (30,388)	$ (96,963)	$ (103,118)

Omega Therapeutics, Inc.
Condensed Consolidated Balance Sheets
(Unaudited, In thousands)

	December 31, 2023	December 31, 2022
Assets		
Cash and cash equivalents	$ 68,443	$ 70,615
Marketable securities	4,986	54,063
Other assets	130,937	21,320
Total assets	**$ 204,366**	**$ 145,998**
Liabilities and stockholders' equity		
Liabilities	$ 146,350	$ 40,027
Stockholders' equity	58,016	105,971
Total liabilities and stockholders' equity	**$ 204,366**	**$ 145,998**

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