Omega Therapeutics Presents New Preclinical Data at AACR 2024 Supporting the Potential of Precision Epigenomic Control

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- *MYC-directed epigenomic controller exerts anti-tumor effect in preclinical models of EGFR inhibitor-resistant NSCLC regardless of underlying resistance mechanism*
- *Validation of novel translational assay enables detection and quantification of site-specific DNA methylation from liquid biopsies to assess target engagement of OTX-2002, our lead clinical-stage epigenomic controller*

CAMBRIDGE, Mass., April 09, 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 the presentation of new preclinical data demonstrating the anti-tumor effect of a MYC-targeting epigenomic controller (MYC-EC) in models of EGFR inhibitor (EGFRi)-resistant non-small cell lung cancer (NSCLC) at the American Association for Cancer Research Annual Meeting 2024, taking place in San Diego, California, April 5 – 10. The Company also presented preclinical data validating a novel pharmacodynamic biomarker assay for monitoring on-target engagement and activity of its clinical-stage EC candidate, OTX-2002.

"We're excited to share these preclinical data at this year's AACR Annual Meeting, which continue to validate Omega's platform," said Thomas McCauley, Ph.D., Chief Scientific Officer of Omega Therapeutics. "These results further underscore the tremendous potential for a MYC-directed epigenomic controller as a novel orthogonal treatment strategy for non-small cell lung cancer as a monotherapy and in combination with existing therapies. More broadly, these data highlight the ongoing progress we have made in demonstrating the immense breadth of potential applicability of our precision epigenomic control approach to advance new programmable mRNA medicines for patients with serious diseases such as cancer."

Abstract 1726: Targeted epigenomic control of MYC as a strategy to treat EGFR inhibitor-resistant NSCLC

Key Findings

- The combination of a MYC-directed EC (NSCLC MYC-EC) with osimertinib, a third generation EGFRi blocker, led to enhanced downregulation of MYC protein levels and synergistically inhibited viability of EGFR-T790M mutant NSCLC cells in preclinical models
- NSCLC cells resistant to osimertinib through the EGFR C797S mutation or epithelial to mesenchymal transition (EMT) retained sensitivity to epigenomic downregulation of MYC expression with NSCLC MYC-EC in multiple *in vitro* models
- These results support potential development of a NSCLC MYC-EC in EGFR-mutant NSCLC as a combination therapy with osimertinib, and as a monotherapy in osimertinib-resistant NSCLC

Abstract 2417: Detection and quantification of site-specific DNA methylation from liquid biopsies as a pharmacodynamic biomarker of OTX-2002, a novel MYC-targeting epigenomic controller

Key Findings

- Development of a new DNA methylation assay consisting of a minimal hybridization capture panel to evaluate CpG methylation events across a ~50 kilobase target region
  - Ultra-sensitive detection of methylation events at the MYC locus down to the theoretical limit of 1 in 10^4 copies of MYC
- Demonstration of highly specific on-target engagement and methylation by OTX-2002 in liquid biopsies from mice bearing human hepatocellular carcinoma (HCC) xenografts

These posters are available on the Omega website at https://omegatherapeutics.com/science/publications.

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.

Forward-Looking Statements

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 potential development of NSCLC MYC-EC in EGFR-mutant NSCLC as a combination therapy with osimertinib, and as a monotherapy in osimertinib-resistant NSCLC, the broad potential of precision epigenomic control, the potential of the Company's pipeline of therapeutic candidates, and upcoming events and presentations. 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; volatility in capital markets and general economic conditions; 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; 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.

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