Omega Therapeutics Showcases Bidirectional and Multiplexed Epigenomic Control of Gene Expression in Preclinical Models of Liver Inflammation and Fibrosis

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First-ever demonstration of sustained pre-transcriptional upregulation of gene expression by an epigenomic controller in both in vitro and in vivo models of liver fibrosis

Single epigenomic controller demonstrated ability to simultaneously regulate the expression of chemokines CXCL9-11 across in vitro models of liver inflammation

CAMBRIDGE, Mass., Nov. 13, 2023 (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 from two different programs that demonstrated sustained upregulation of gene expression and coordinated pre-transcriptional downregulation of multiple genes in models of liver fibrosis and inflammation, respectively, at the American Association for the Study of Liver Diseases' (AASLD) The Liver Meeting® 2023, taking place in Boston, Massachusetts, November 10 – 14.

"Genetic medicines have made tremendous progress towards precise downregulation of gene expression. However, to extend their reach, we need to bidirectionally control the expression of multiple genes simultaneously," said Thomas McCauley, Ph.D., Chief Scientific Officer of Omega Therapeutics. "We believe that these new data demonstrate the power of our programmable epigenomic mRNA development candidates to control gene expression with unmatched flexibility. To our knowledge, these are the first results to show how site-specific epigenomic modulation can durably upregulate the expression of a master liver regeneration gene. Additionally, a second poster highlights our ability to multiplex gene regulation with a single construct to control a cluster of inflammatory chemokines. These exciting results highlight the progress we have made and possible applications of our approach in multiple liver diseases."

Poster 3444-A: Induction of Hepatocyte Nuclear Factor 4 alpha (HNF4α) using novel epigenomic controllers

Key Findings

- Human cell lines treated with an epigenomic controller (EC) engineered to modulate the epigenetic profile of the P1 promoter of the HFN4α gene, a master regulator of liver development and function, showed strong increases of mRNA and protein levels.
- Upregulation of HFN4α expression following a single EC treatment persisted for ≥10 days and induced strong and durable increases in HNF4α mRNA levels in primary human hepatocytes.
- EC-mediated upregulation of HNF4α expression correlated with significantly reduced expression of clinically relevant fibrotic genes *in vitro.*
- Single administration of an EC in the humanized FRG mouse model resulted in induction of HNF4α mRNA levels compared to untreated FRG mice.
- EC-mediated induction of HNF4α expression *in vivo* in a mouse model of liver fibrosis led to decreased collagen deposition, a key marker of fibrosis.
    - Regulation of HNF4α also led to changes in expression of other fibrosis-associated genes.

Poster 2621-A: Targeting CXCL9/CXCL10/CXCL11 using novel epigenomic controllers for the treatment of inflammatory liver disease

Key Findings:

- Treatment of mouse and human liver cells with ECs engineered to pre-transcriptionally downregulate the expression CXCL9, CXCL10 and CXCL11 resulted in robust mRNA downregulation and decreased protein levels of all three chemokines.
- Primary human hepatocytes stimulated with interferon gamma (INFG) and treated with a single EC targeting CXCL9-11 resulted in a statistically significant decrease in mRNA expression and protein levels of each chemokine compared to INFG stimulation alone.
- Human T cells exposed to conditioned media from primary human hepatocytes treated with INFG and an EC targeting CXCL9-11 displayed 75% reduced migration compared to cells treated with INFG alone.

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 controlled epigenomic modulation 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 diverse pipeline of therapeutic candidates derived from its OMEGA platform spanning oncology, regenerative medicine, multigenic diseases including immunology, and select monogenic diseases.

For more information, visit omegatherapeutics.com, or follow us on X (formerly Twitter) and LinkedIn.

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 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; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 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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