Omega Therapeutics Announces the Industry's First Programmable Epigenetic Medicine in Development and 2021 Priorities

OTX-2002 To Be Developed for the Treatment of MYC-Driven Hepatocellular Carcinoma

Company is Advancing Candidate Into IND-Enabling Studies, with the Goal of Commencing a Phase 1/2 Clinical Trial Thereafter

CAMBRIDGE, Mass., January 13, 2021 – Omega Therapeutics, Inc. ("Omega"), a development-stage biotechnology company pioneering the field of epigenomic programming to precisely regulate and control the epigenetics of the human genome to treat and cure disease, today announced that it has selected its first Omega Epigenomic Controller™ development candidate OTX-2002 to advance into Investigational New Drug (IND)-enabling studies.

Omega scientists rationally designed OTX-2002 as a novel, engineered therapeutic to specifically control c-myc (MYC) oncogene expression and demonstrated its effect in hepatocellular carcinoma (HCC). Preclinical animal studies show OTX-2002 potently down-regulates MYC. Successfully creating a way to control MYC expression in cancer has historically eluded the efforts of many groups.

"Our science and pipeline made tremendous progress in 2020. Our platform yielded a pipeline of eight novel epigenetic targets and corresponding epigenomic controllers with the potential to address a wide range of high unmet need diseases, including HCC, non-small cell lung cancer (NSCLC), end-stage liver disease (ESLD), acute respiratory distress syndrome (ARDS), and alopecia," said Mahesh Karande, President and Chief Executive Officer, Omega Therapeutics. "Based on the power of our platform, our MYC program may represent a breakthrough for direct, tunable modulation of the MYC oncogene. As we look ahead, we plan to unveil several more development candidates during 2021, and plan to have multiple development candidates in the clinic thereafter."

Omega's platform interrogates the three-dimensional architecture of the human genome to identify DNA targets that reflect druggable areas of distinct and conserved structures called Insulated Genomic Domains (IGDs). We then design proteins, Omega Epigenomic Controllers™, which drug these DNA targets to control the epigenetic state of a specific gene or genes in the human genome. We deploy our epigenomic controllers using mRNA and lipid nanoparticles (LNPs) and then deliver them via either intravenous, subcutaneous, topical, and other routes.

"We founded Omega Therapeutics to therapeutically control nature's own operating system for gene regulation and cell differentiation. The team made immense progress in a completely new area of biology and has nominated its first Omega Epigenomic Controller™ product development candidate in a

historically undruggable target of oncology. I am very pleased with Omega's progress as we develop the Company's pioneering epigenomic programming platform designed to treat and cure diseases by tackling undruggable targets, multigenic complex diseases and cellular programming," said Noubar Afeyan, Ph.D., Chief Executive Officer of Flagship Pioneering and Co-founder and Chairman of the Board for Omega Therapeutics.

"Despite recent advancements, there remains a substantial need for new therapies with new mechanisms of action for difficult to treat cancers. The MYC oncoprotein plays a pivotal role in tumor cell proliferation and downstream growth signaling of many, perhaps most cancers but has hitherto been considered undruggable. However, it is precisely down-regulated by Omega's OTX-2002, an exciting breakthrough with the potential to redefine cancer treatment. Preclinical studies in HCC models using OTX-2002 have demonstrated promising preclinical dose-responsive tumor inhibition and superior safety profiles compared to small molecule standards of care. These encouraging results warrant continued research into the utility of modulating MYC by administration of OTX-2002 and speak to the drug's potential as a new treatment for HCC," said Gerard Evan, Ph.D., FRS, FMedSci, Sir William Dunn Professor of Biochemistry and Head of the Department of Biochemistry, University of Cambridge.

Omega's President and Chief Executive Officer, Mahesh Karande, will provide an overview of the Company's platform, strategy and recent progress in a virtual presentation taking place today, January 13, 2021 at 9:50 a.m. ET at the 39th Annual J.P. Morgan Healthcare Conference.

OTX-2002 for the Treatment of HCC and Program Priorities

The oncogene MYC is a master transcription factor that regulates cell proliferation, differentiation and apoptosis and plays a significant role in more than 50% of all human cancers. Genetic analysis conducted by others has revealed that MYC over-expression is present in up to 70% of viral and alcohol-related HCC. Preclinical studies have shown OTX-2002 decreases the expression of MYC, despite this gene being previously known as an undruggable target. This breakthrough could provide potentially safer and more efficacious treatment options for patients and transform the practice of medicine in oncology.

- Commence IND-enabling studies
- Submit IND to the U.S. Food and Drug Administration (FDA)
- Initiate Phase 1/2 clinical study

Other Near-Term Candidates

Omega has a rich pipeline and is developing novel therapeutics to address a wide range of disease categories. In 2021, Omega expects to name several additional development candidates targeting indications including inflammatory diseases, ARDS associated with COVID-19, alopecia, neutrophilic dermatoses, NSCLC and an additional oncogene target. These candidates are designed to address diseases driven by dysregulation of single or multiple genes, master regulatory genes, and historically difficult to drug gene targets.

About Omega Epigenomic Controllers™ and Omega Epigenomic Programming™

Omega Therapeutics is developing a new class of engineered and modular therapeutics, called Omega Epigenomic Controllers™, that can be programmed to precisely downregulate or upregulate the level of expression of any of the 25,000+ human genes, individually or collectively, with controlled durability, to

treat and potentially cure disease. Omega Epigenomic Programming™ represents an entirely new and breakthrough approach, allowing the Company's product candidates to drug previously undruggable targets across a broad range of diseases. The foundation of Omega's platform lies within the three-dimensional architecture of the human genome and its accompanying regulators, which are organized into distinct and conserved structures called Insulated Genomic Domains (IGDs). Omega's technology exploits the topology and functionality of these IGDs as druggable targets to activate the genome's innate ability to treat and cure disease. Omega's medicines are being developed to be dosed only as frequently as therapeutically necessary by intervening at the pre-transcriptional level and function without altering the native human genetic code or nucleic acid sequences.

About Omega Therapeutics

Omega Therapeutics is a privately held, development-stage biotechnology company pioneering the field of epigenomic programming to precisely regulate and control the human genome to treat and cure disease. Omega's breakthrough science has enabled it to tap into nature's universal operating system, that epigenetically controls the human genome, to target the most fundamental genomic processes which fuel cellular growth, differentiation, and gene expression. Omega Therapeutics was founded by Flagship Pioneering in 2017 and currently has eight programs in various stages of preclinical development. The Company is strategically pursuing specific disease targets that have not been successfully addressed through conventional modalities, including certain oncology indications, liver disease, serious inflammatory conditions, and acute respiratory distress syndrome (ARDS) among others. Omega's mission is to transform medicine and deliver the therapies of tomorrow.

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

Investor contact:
Joseph Rayne
Argot Partners
212.600.1902
joseph@argotpartners.com

Media contact:
David Rosen
Argot Partners
212.600.1902
david.rosen@argotpartners.com