Omega Therapeutics Reports Second Quarter 2022 Financial Results and Highlights Recent Company Progress

August 4, 2022

- *FDA Clearance of IND Application for OTX-2002, the First Ever Epigenomic Controller, for MYC Driven Hepatocellular Carcinoma Received*
- *Launch of Phase 1/2 Clinical Trial Under the MYCHELANGELO™ Clinical Program in Patients Expected in 2H'22*
- *Data from Preclinical Studies Show Promising Anti-Tumor Activity and Loss of Cancer Cell Viability Achieved Through Pre-Transcriptional Downregulation of MYC Gene Expression*
- *$173.7 Million in Cash, Cash Equivalents and Marketable Securities at End of Second Quarter*

CAMBRIDGE, Mass., Aug. 4, 2022 /PRNewswire/ -- Omega Therapeutics, Inc. (Nasdaq: OMGA) ("Omega"), a clinical-stage biotechnology company pioneering the first systematic approach to use mRNA therapeutics as a new class of programmable epigenetic medicines by leveraging its OMEGA Epigenomic Programming™ platform, today announced financial results for the second quarter ended June 30, 2022, and highlighted recent Company progress.

"This has been an exciting second quarter for Omega, in which we were thrilled to receive FDA clearance of our first IND application for OTX-2002, representing the first ever Omega Epigenomic Controller™, a new class of programmable mRNA therapeutics. This is a critical milestone for Omega as we enter our next phase of growth and reflects our pioneering work to realize the potential of epigenomic programming," said Mahesh Karande, President and Chief Executive Officer of Omega Therapeutics. "Additionally, we were also pleased to share exciting, new supportive preclinical data, both from our lead program OTX-2002 in hepatocellular carcinoma, as well as from another program in our pipeline focused on non-small cell lung cancer, a potential future indication. We look forward to continuing this momentum as we enter the clinic in the second half of this year and further exploring the broad ranging capabilities of our novel platform in additional therapeutic areas."

Recent Business Highlights

Development Pipeline and Platform

- **Received FDA Clearance of Investigational New Drug (IND) application for OTX-2002, the First Omega Epigenomic Controller™ (OEC), for MYC driven Hepatocellular Carcinoma (HCC):** OTX-2002 is a novel, engineered, and programmable mRNA therapeutic designed to downregulate c-Myc (MYC) expression pre-transcriptionally through epigenetic modulation while potentially overcoming MYC autoregulation. This represents the first ever epigenomic controller, a new class of programmable mRNA therapeutics, to receive IND clearance.
- **On Track to Launch a Phase 1/2 Clinical Trial Under the MYCHELANGELO™ Clinical Trial Program in HCC patients in the 2H'22:** The study consists of Part 1 (OTX-2002 as monotherapy) and Part 2 (OTX-2002 combined with standards of care in HCC). The Phase 1/2 trial will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of OTX-2002 as a monotherapy and in combination with standard of care therapies in patients with relapsed or refractory HCC and other solid tumor types known for association with the MYC oncogene. The study is expected to enroll approximately 190 patients at clinical trial sites in the United States, Asia, and Europe and the Company expects to dose the first patient during the fourth quarter of 2022.
    - **Part 1:** This dose escalation portion of the trial will evaluate OTX-2002 monotherapy in patients with relapsed or refractory HCC and other solid tumors. Investigators will utilize a 3+3 design to identify the following primary endpoints of any dose limiting toxicities (DLTs), maximum tolerated dose (MTD), incidence of treatment emergent adverse events (TEAEs), and the recommended dose for expansion (RDE). There will then be a monotherapy expansion for patients with relapsed or refractory HCC who have received at least 1 prior line of systemic anticancer treatment and are without available subsequent standards of care. These patients will receive the RDE of OTX-2002. The primary endpoints of the monotherapy expansion will be overall response rate (ORR) and duration of response (DOR).
    - **Part 2:** This portion of the trial will evaluate OTX-2002 in combination with standard of care therapies and will consist of safety run-in and expansion cohorts. During the safety run-in, patients with relapsed or refractory HCC will receive OTX-2002 at the selected dose in combination with one of three current standard of care therapies. These combination partners will be one of two types of tyrosine kinase inhibitors (TKIs) or an immune checkpoint inhibitor (ICI). The primary endpoints of the safety run-in will be DLT, MTD, and incidence of TEAEs. Once the combination therapies have been determined to be tolerable in the safety run-in, patients with relapsed or refractory HCC will be enrolled into the expansion cohorts for each of the combination therapies, with the primary endpoints

of ORR and DOR.

- **New OTX-2002 Preclinical Data Presented at Three Major Medical Meetings Show Robust *In Vivo* Efficacy and *In Vitro* Loss of Cancer Cell Viability:**
  - **Non-Human Primate (NHP) Data for OTX-2002 in HCC Presented at ESMO-GI 2022:** Results showed that treatment with OTX-2002 resulted in robust *in vivo* efficacy in xenograft tumor models and successfully achieved pre-transcriptional downregulation of hepatocyte MYC gene expression in NHPs. These data support the clinical potential of OTX-2002 in combination with existing standard of care therapies for HCC, including ICIs. The ESMO-GI poster presentation is available here.
  - ***In Vivo* Data for OTX-2002 in HCC Presented at AACR 2022:** Results demonstrated that OTX-2002 suppresses MYC gene expression resulting in a loss of cancer cell viability *in vitro* and a reduction in tumor growth in *in vivo* xenograft models. These data support the potential of Omega's platform to engineer programmable mRNA therapeutics that successfully regulate gene expression. The AACR poster presentation is available here.
  - ***In Vivo* OEC Data in Models of Non-Small Cell Lung Cancer (NSCLC) Presented at ASGCT 2022:** Results demonstrated that regulation of MYC gene expression via epigenomic programming resulted in decreased viability of cancer cells *in vitro* and reduced tumor burden in *in vivo* xenograft models. These data support the potential of OECs to precisely and durably regulate gene expression and their potential as a future treatment for NSCLC. The ASGCT poster presentation is available here.
- **Additional OEC Development**: Beyond HCC and NSCLC, the Company is advancing multiple programs through preclinical studies spanning oncology, multigenic diseases including immunology, regenerative medicine, and select monogenic diseases.
- **OMEGA Epigenomic Programming™ Platform:** Omega is creating a new generation of programmable mRNA medicines that are designed to control the fundamental epigenetic processes to correct the root cause of disease by restoring aberrant gene expression to normal levels without altering native nucleic acid sequences. Omega has developed a highly rational and deterministic approach to drug design that enables the Company to rapidly develop and optimize novel OECs with high target specificity to durably tune the expression of single or multiple genes. Omega is advancing multiple preclinical development programs spanning oncology, multigenic diseases including immunology, regenerative medicine, and select monogenic diseases.

Corporate

- **Joshua Reed Appointed Chief Financial Officer**. Mr. Reed brings over 25 years of successful and diverse corporate and financial operations experience including capital raising, business development, and investor relations.

Second Quarter 2022 Financial Results

As of June 30, 2022, the Company had cash, cash equivalents and marketable securities totaling $173.7 million.

Research and development (R&D) expenses for the second quarter of 2022 were $19.4 million, compared to $11.2 million for the second quarter of 2021. The $8.2 million increase in R&D expense was primarily driven by an increase in personnel-related expenses, external manufacturing costs, and study costs in support of the advancement of our programs

General and administrative (G&A) expenses for the second quarter of 2022 were $6.2 million, compared to $3.6 million for the second quarter of 2021. The $2.6 million increase in G&A expense was primarily driven by an increase in personnel-related expenses to support business growth.

Net loss for the second quarter of 2022 was $25.9 million, compared to $15.4 million for the second quarter of 2021, driven predominantly by increased R&D and G&A expenses to support the Company's growth and operations as a public company.

About Omega Therapeutics

Omega Therapeutics, founded by Flagship Pioneering, is a clinical-stage biotechnology company pioneering the first systematic approach to use mRNA therapeutics as a new class of programmable epigenetic medicines. The company's OMEGA Epigenomic Programming™ platform harnesses the power of epigenetics, the mechanism that controls gene expression and every aspect of an organism's life from cell genesis, growth, and differentiation to cell death. Using a suite of technologies, paired with Omega's process of systematic, rational, and integrative drug design, the OMEGA platform enables control of fundamental epigenetic processes to correct the root cause of disease by returning aberrant gene expression to a normal range without altering native nucleic acid sequences. Omega's modular and programmable mRNA medicines, Omega Epigenomic Controllers™, are designed to target specific epigenomic loci within insulated genomic domains, EpiZips, from amongst thousands of unique, mapped, and validated genome-wide DNA-sequences, with high specificity to durably tune single or multiple genes to treat and cure diseases through Precision Genomic Control™. Omega is currently advancing a broad pipeline of development candidates spanning a range of disease areas, including oncology, regenerative medicine, multigenic diseases including immunology, and select monogenic diseases, including alopecia.

For more information, visit omegatherapeutics.com, or follow us on **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 timing and design of our Phase 1/2 MYCHELANGELO™ clinical trial; the potential of the OMEGA platform to engineer programmable epigenetic mRNA therapeutics that successfully regulate gene expression by targeting insulated genomic domains;

expectations surrounding the potential of our product candidates, including our lead OEC candidate OTX-2002; and 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. 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 controller machines 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 OEC 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 June 30, 2022, 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.

Investor contact:
Kevin Murphy
Argot Partners
212.600.1902
ArgotOmega@argotpartners.com

Media contact:
Jason Braco, Ph.D.
LifeSci Communications
646.751.4361
jbraco@lifescicomms.com

Omega Therapeutics, Inc.
Condensed consolidated statements of operations and comprehensive loss
(thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Collaboration revenue from related party	$ 476	$ —	$ 743	$ —
Operating expenses:				
Research and development	19,387	11,184	33,659	20,933
General and administrative	6,202	3,637	11,336	6,452
Related party expense, net	741	384	1,562	763
Total operating expenses	26,330	15,205	46,557	28,148
Loss from operations	(25,854)	(15,205)	(45,814)	(28,148)
Other expense, net:				
Interest expense, net	(55)	(190)	(210)	(402)
Change in fair value of warrant liability	—	(11)	—	(340)
Other expense, net	(3)	(4)	(52)	(8)
Total other expense, net	(58)	(205)	(262)	(750)
Net loss	$ (25,912)	$ (15,410)	$ (46,076)	$ (28,898)
Net loss per common stock attributable to common stockholders, basic and diluted	$ (0.54)	$ (3.36)	$ (0.96)	$ (6.36)
Weighted-average common stock used in net loss per share attributable to common stockholders, basic and diluted	47,849,639	4,588,500	47,828,594	4,542,832
Comprehensive loss:				
Net loss	$ (25,912)	$ (15,410)	$ (46,076)	$ (28,898)
Other comprehensive loss:				
Unrealized loss on marketable securities	(147)	—	(944)	—
Comprehensive loss	$ (26,059)	$ (15,410)	$ (47,020)	$ (28,898)

Omega Therapeutics, Inc.
Condensed Consolidated Balance Sheets

(thousands)

	June 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 90,857	$ 186,482
Marketable securities	82,808	38,845
Other assets	19,381	8,006
Total assets	**$ 193,046**	**$ 233,333**
Liabilities and stockholders' equity		
Liabilities	$ 35,662	$ 32,705
Stockholders' equity	157,384	200,628
Total liabilities and stockholders' equity	**$ 193,046**	**$ 233,333**

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