# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2022**

**OR**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

**Commission File Number 001-40657**

# Omega Therapeutics, Inc.

**(Exact name of Registrant as specified in its Charter)**

| **Delaware** | **81-3247585** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **20 Acorn Park Drive Cambridge, MA** | **02140** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (617) 949-4360**

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common stock, par value $0.001 per share | OMGA | The Nasdaq Global Select Market |

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☐ |
| Non-accelerated filer | ☒ | Smaller reporting company | ☒ |
| | | Emerging growth company | ☒ |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

At June 30, 2022, the last business day of the Registrant's most recently completed second fiscal quarter, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was approximately $80.0 million. Solely for purposes of this disclosure, shares of

common stock held by executive officers, directors and certain stockholders of the Registrant as of such date have been excluded because such holders may be deemed to be affiliates.

The number of shares of Registrant's Common Stock outstanding as of February 24, 2023 was 48,095,462.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement relating to its 2023 Annual Meeting of Stockholders, to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2022, are incorporated herein by reference in Part III.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, the sufficiency of our cash, cash equivalents and marketable securities to fund our operating expenses and capital expenditure requirements, business strategy, product candidate development, prospective products, product candidate approvals, research and development activities and costs, future revenue, timing and likelihood of success of our business plans, plans and objectives of management, future results and timing of clinical trials, treatment potential of our product candidates, and the market potential of our product candidates are forward-looking statements. These statements 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.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," "would" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. The forward-looking statements in this Annual Report are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under Part I, Item 1A. "Risk Factors" in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

As used in this Annual Report, unless otherwise stated or the context requires otherwise, references to "Omega," "Omega Therapeutics," the "Company," "we," "us," and "our," refer to Omega Therapeutics, Inc. and its subsidiary on a consolidated basis.

## SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. “Risk Factors” in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- Our product candidates are based on a novel technology, which makes it difficult to predict the time and cost of preclinical and clinical development and of subsequently obtaining regulatory approval, if at all.
- No epigenomic controller medicines have been approved in this potentially new class of medicines, and may never be approved as a result of efforts by others or us. mRNA drug development has substantial development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.
- We have a limited operating history and no history of successfully developing or commercializing any approved product candidates, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.
- We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future.
- We require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce, or terminate our product development.
- We have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. Such investments may affect our operating results, and, if the return on these investments is lower or develops more slowly than we expect, our revenue and operating results may suffer.
- Preclinical development is uncertain, especially for a new class of medicines such as epigenomic controllers, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance into the clinic, any of which may have a material adverse impact on our platform or our business.
- Our product candidate, OTX-2002, was recently cleared by the United States Food and Drug Administration to advance to clinical development. Clinical development of OTX-2002 may be delayed or terminated, and we may never obtain regulatory approval of OTX-2002, which may have a material adverse impact on our platform or our business. Furthermore, clinical development requires substantial capital investment, which we may not be able to support. We may incur unforeseen costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of OTX-2002 and our other product candidates.
- Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.
- Our ability to manufacture our Omega Epigenomic Controller™ candidates, or OEC candidates, for preclinical or clinical supply could be limited, especially with the increased demand for the manufacture of mRNA- and LNP-based vaccines to treat COVID-19, which could adversely affect our development plans.
- Our OEC candidates are based on novel technology and may be complex and difficult to manufacture. We may encounter difficulties in manufacturing, product release, shelf life, testing, storage, supply chain management or shipping.
- We must adapt to rapid and significant technological change and respond to introductions of new products and technologies by competitors to remain competitive.
- We will rely on third parties for the foreseeable future for the manufacture and supply of materials for our research programs, preclinical studies and clinical trials and we do not have long-term contracts with many of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, including drug supplies for combination therapy, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.
- We continue to evaluate plans to acquire and establish our own manufacturing facility and infrastructure in addition to or in lieu of relying on contract development and manufacturing organizations for the manufacture of

our product candidates. Any plan to establish our own manufacturing facility and infrastructure will be costly and time-consuming and we may not be successful.

- We have a limited number of suppliers for the lipid excipients used in our product candidates and certain of our suppliers are critical to our production. If we were to lose a critical supplier, it could have a material adverse effect on our ability to complete the development of our product candidates. If we obtain regulatory approval for any of our product candidates, we would need to expand the supply of lipid excipients in order to commercialize them.
- We are very early in our development efforts. Most of our product candidates are in preclinical development or discovery, and we recently received FDA clearance for our IND application for OTX-2002 and have initiated the associated clinical trial. It will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- If we are unable to obtain, maintain, enforce and adequately protect our intellectual property rights with respect to our technology and product candidates, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.
- Third parties may obtain or control intellectual property rights that may prevent or limit the development of our technology or products. Third-party claims of intellectual property infringement, misappropriation or other violation may result in substantial costs or prevent or delay our development and commercialization efforts.

## PART I

### Item 1. Business.

#### Overview

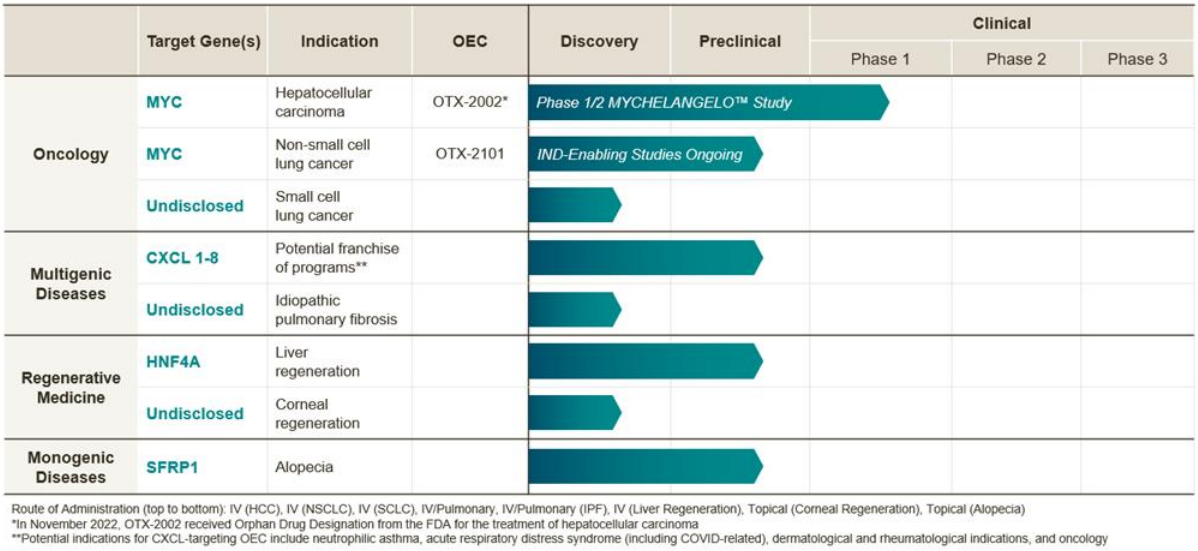
Omega Therapeutics is a clinical-stage biotechnology company pioneering the development of a new class of programmable epigenetic mRNA medicines. Our OMEGA platform harnesses the power of epigenetics and our deep understanding of genomic architecture to precisely target and controllably modulate gene expression at the pre-transcriptional level to treat or cure diseases. We have deciphered the three-dimensional architecture of the human genome. Genes and their accompanying regulators are organized into distinct and evolutionarily conserved structures called Insulated Genomic Domains, or IGDs. IGDs are the fundamental structural and functional units of gene control and cell differentiation and collectively act as nature's innate control system. Most diseases are caused by aberrant gene expression rooted in alterations in IGDs. The OMEGA platform has enabled us to systematically identify and validate thousands of novel and unique DNA-sequence-based epigenomic "zip codes" associated with individual regulatory elements within IGDs. We call these epigenomic targets EpiZips. We rationally design and engineer our mRNA therapeutics, which are programmable and modular epigenetic medicines, called Omega Epigenomic Controllers, or OECs, to target EpiZips for Precision Epigenomic Control. This enables us to precisely tune genes to a desired level of expression and to control the duration of expression. Through this approach, we believe that the OMEGA platform has broad potential applicability across a range of diseases, processes and conditions. Our pipeline currently consists of early-stage programs that span oncology, multigenic diseases including immunology, regenerative medicine, and select monogenic diseases.

We believe that the Precision Epigenomic Control delivered by the OMEGA platform has broad therapeutic applicability and transformational potential, initially spanning across:

- ***Oncology.*** Control of target oncogenes including historically challenging, auto-regulatory or un-druggable targets in various cancers.
- ***Multigenic diseases including immunology.*** Regulation of multiple genes within an IGD or across IGDs.
- ***Regenerative medicine.*** Recapitulation of developmental and mature-state gene expression to drive cellular regeneration and restore normal function.
- ***Select monogenic diseases.*** Correction of dysregulation in monogenic rare and non-rare diseases.

## Our Pipeline

Our current pipeline consists of the following programs:




Route of Administration (top to bottom): IV (HCC), IV (NSCLC), IV (SCLC), IV/Pulmonary, IV/Pulmonary (IPF), IV (Liver Regeneration), Topical (Corneal Regeneration), Topical (Alopecia)
*In November 2022, OTX-2002 received Orphan Drug Designation from the FDA for the treatment of hepatocellular carcinoma
**Potential indications for CXCL-targeting OEC include neutrophilic asthma, acute respiratory distress syndrome (including COVID-related), dermatological and rheumatological indications, and oncology

## Intellectual Property and Manufacturing Capabilities

We have consolidated a significant intellectual property estate covering the OMEGA platform and our OECs through our own development activities and through licenses from the Whitehead Institute at the Massachusetts Institute of Technology, or the Whitehead Institute. We are also developing internal and external manufacturing capabilities, including evaluating plans to build our own facility, to provide appropriate scale and quality to support development and commercialization of our OECs.

## Our Strategy

Our objective is to become the leading programmable epigenetic medicines company by engineering, developing, manufacturing, and commercializing OECs, utilizing the OMEGA platform. Our vision is to treat and cure serious diseases by selectively and safely directing the human genome to control gene expression pre-transcriptionally without altering native DNA sequences.

Our strategy includes:

- ***Strategically invest in and advance the OMEGA platform***. Our scientific and technical expertise and expansive intellectual property estate have enabled us to develop our industry-leading, pioneering OMEGA platform. We plan to continue to invest in expanding our knowledge of IGD biology and epigenetics in order to identify new DNA-sequence-based epigenomic targets, the EpiZips, further our capacity to innovate and engineer OECs, expand our technologies, broaden our delivery capabilities, and enhance our institutionalized knowledge to further solidify our position as a leading digital and data-driven epigenetic medicines company. We plan to build additional computational, big-data, and advanced-analytic capabilities to maintain our leadership position. We plan to expand and strengthen our position as leaders in developing mRNA therapeutics for epigenomic control.
- ***Establish OECs as a new class of programmable epigenetic mRNA medicines.*** Through the breadth of our research-and-development activities and the pursuit of high-value biological targets, we seek to demonstrate the unprecedented therapeutic potential of our OECs and to expand our repertoire of OECs that can be used for therapeutic applications. We have conducted *in vivo* preclinical studies of

our OECs in multiple disease models for various indications, including hepatocellular carcinoma, or HCC, non-small cell lung cancer, or NSCLC, and acute respiratory distress syndrome, or ARDS, and we expect to conduct *in vivo* preclinical studies for multiple additional programs. We have initiated clinical development for the HCC program and IND-enabling studies for our NSCLC program.

- ***Expand our pipeline through internal and partnering efforts.*** We believe the OMEGA platform can be used to create therapeutics to treat a broad array of human diseases by regulating the expression of single or multiple genes. Internally, we intend to focus our development and commercialization efforts in areas of high unmet need with well-defined and circumscribed patient populations. At the same time, we plan to seek collaborations or co-development arrangements to mitigate development risk or gain access to novel delivery technologies.
- ***Build a fully integrated digitalized biopharmaceutical company.*** Our intent is to develop a world-class biopharmaceutical company by leveraging our innate and differentiated platform attributes and digitalized end-to-end capabilities across research, discovery, preclinical and clinical development, manufacturing, and commercial operations. We believe the integrated and modular nature of the OMEGA platform enables iterative learnings and insights for efficient, evidence-based decision making to optimize the engineering, development, and selection of our OEC candidates.
- ***Curate world-class talent and culture.*** Our culture is guided by our overarching ethos: Ambitious, yet humble. Our unparalleled motivation to transform human medicine through our pioneering work is combined with our underlying sense of humility, which is essential for keeping patients front and center. Given the pioneering nature of our business, identifying, nurturing, developing, and retaining leading talent is a critical element of our strategy.

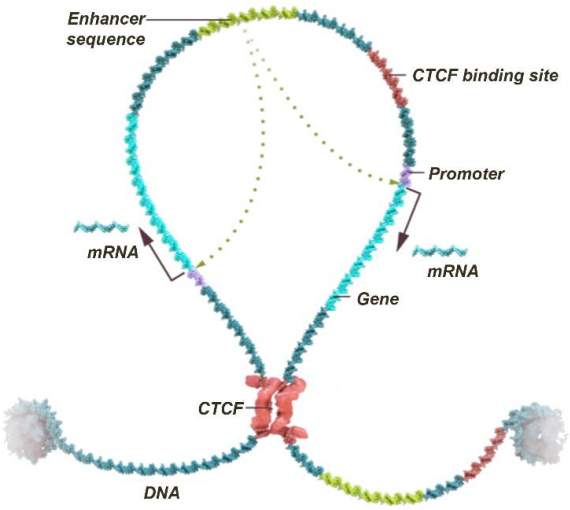
**Background on Insulated Genomic Domains (IGDs)**

Epigenetics is the mechanism that systematically controls every aspect of an organism's life from cell growth and differentiation to cell death. Our team has developed an understanding of the universal operating system of epigenetics and has built the OMEGA platform to replicate nature's method of gene control for therapeutic benefit. IGDs are key to understanding the organization of this operating system and act as the fundamental structural and functional units of gene control and cell differentiation. There are approximately 15,000 IGDs that encompass the roughly 20,000 genes that are distributed across our 23 chromosomes. They are ubiquitous in every cell and evolutionarily conserved within and largely across species.

Gene expression in cells is generally controlled by a highly diverse class of regulatory elements, such as enhancers, repressors and promoters. These regulatory elements are relatively short segments of DNA that act as binding sites for protein transcription factors that in turn recruit other proteins to activate transcription of targeted genes. Current research indicates that genes and their associated regulatory elements reside in a modular fashion within IGDs. The chromosomal-looping structure of IGDs ensures that interactions between genes and their regulatory elements are insulated from neighboring IGDs and extraneous regulatory factors, which is critical for ensuring normal cell-specific gene regulation. The CCCTC-binding factor, CTCF, and the cohesin complex are critical players in the formation and maintenance of the IGD structure. Cohesin is the motor

that extrudes and enlarges the IGD loop, while CTCF blocks cohesin from further extrusion and acts as an anchor, thereby enforcing boundaries between IGDs.

**Graphical Representation of an IGD**




IGDs encompass protein-coding genes and their regulatory elements. A single IGD typically contains between one and ten genes, with a median of three genes. Epigenomic controllers are designed to affect the expression of genes within specific IGDs through precise modulation of one or more IGD components (EpiZips) to control gene expression. Controllers can also be multiplexed to target multiple IGDs.

Any perturbation of an IGD or its boundary has the potential to cause the dysregulation of one or all genes inside it, giving rise to a range of disease states. Alterations of IGDs, which can be either structural or functional in nature, include mutations or disruptions in anchor-CTCF binding sequences, gene promoters, and enhancer regions (including super-enhancers). For example, mutations in the coding sequences for CTCF and cohesin have been observed in various solid-tumor cancers, including breast, prostate, and kidney cancer, as well as in leukemia. IGD boundary alterations may consist of the aberrant inclusion or exclusion of regulatory elements or genes. For example, in some cancers, disruption of the IGD boundary can rewire loop interactions to include strong activating regulatory elements called super-enhancers to upregulate an oncogene. Similar activation can be found in cases of genetic inversion and translocation. Epigenomic changes at the IGD boundary, for example aberrant DNA methylation, can alter CTCF binding and lead to gene exclusion or expose genes within the IGD to external regulatory elements. Pathological evidence of this disruption has been identified in cancers, such as gliomas, and in inherited human diseases, such as Fragile X syndrome.

**OMEGA Platform**

We believe that the OMEGA platform represents an unprecedented approach to developing therapeutics to treat the epigenetic basis of disease by precisely controlling gene expression without altering native DNA sequences. We believe that our OECs' ability to precisely target and provide controlled tunable and durable effects has the potential to treat a wide range of diseases.

The OMEGA platform consists of four pillars.

***1. Proprietary Database of IGDs and EpiZips***

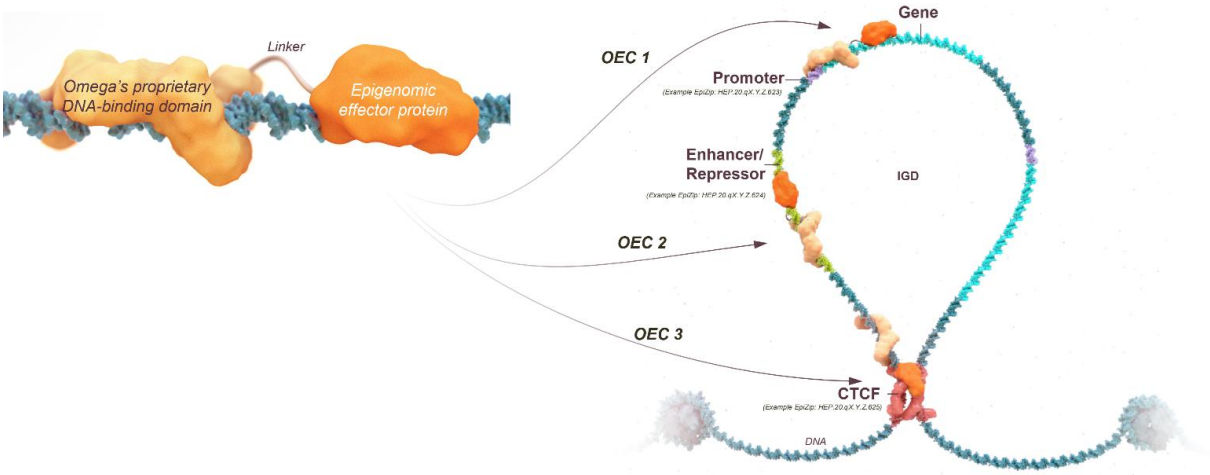
We utilize a biology-first approach to target identification starting with validated gene targets linked to a disease indication of interest. We use proprietary algorithms and machine-learning tools to mine our own and

public databases to develop a comprehensive profile of the target IGD to understand how it is dysregulated in diseased states. We synthesize this information to determine the key therapeutic intervention points, the EpiZips, to be targeted with OECs to achieve the desired effect on gene expression. Through this process, we have built an expansive library of thousands of EpiZips and IGDs as potential therapeutic targets.

### *2. Programmable and Modular Epigenetic mRNA Medicines (OECs) Tailored to Disease*

We have created a modular basis for efficient and intelligent design of programmable epigenetic medicines, the OECs. These prospectively engineered investigational medicines allow us to regulate multiple genes with exquisite specificity, controllable tuning, and duration of effect. Our OECs are programmable mRNA therapeutics that express fusion proteins comprised of two components—a DNA-binding domain and an epigenomic effector protein, as shown in the figure below. The DNA-binding domain is designed to target a particular EpiZip with exquisite specificity. The epigenomic effector protein is designed to interact with DNA or DNA-associated proteins within the cell nucleus, such as histones and transcription factors, to up- or down-regulate gene expression and control the duration of effect. We use proprietary algorithms to design our OECs, including programming DNA-binding domains and selecting optimal epigenomic effector proteins. These computational tools allow us to efficiently generate numerous potential OECs and increases our ability to engineer OECs to treat a particular target.

**Omega Epigenomic Controller (OEC)***




*mRNA medicines expressed as proteins in cell nucleus

We are currently developing proprietary zinc-finger-like proteins and other DNA-binding domains. For epigenomic effectors, we have generated and continue to build a library consisting of more than 100 single- and multi-functional epigenomic effector domains, including both naturally occurring and proprietary engineered variants of DNA-modifying factors, histone-modifying factors, and other chromatin-remodeling factors.

The initial identification of IGDs, EpiZips, and the mechanism of action for OECs directed to particular target genes are rapidly validated utilizing epigenomic controller screens. Our modular design approach allows us to accelerate our discovery process and to identify gene targets and generate initial lead OECs to modulate them in potentially as little as a few weeks.

### *3. Engineered, Customized Drug Delivery to Target Tissues and Cells*

Delivery to the appropriate cells and tissues is critical to the successful application of our technology. We are exploring and innovating a multitude of delivery methods.

We have chosen lipid-nanoparticle-, or LNP-, delivery technology validated in third-party clinical trials for our initial programs. LNPs are currently used in products, both approved and in development. We have deep expertise in delivery formulations and leverage technological improvements and established regulatory precedents to develop our own LNPs. We are delivering our OECs as mRNA, which encodes the DNA binding domain and epigenetic effector proteins, encapsulated within a LNP. Our LNPs are typically 3- or 4-component molecules that encapsulate nucleic acids like mRNA, protect and transport them to organs and tissues within the body, and facilitate their uptake into cells. We believe our LNPs are capable of providing re-dosable, non-viral, *in vivo* delivery to the liver, lung, central nervous system, immune cells, joints, and other cells and tissues. Once taken up into cells, the LNP enables release of the mRNA cargo into the cytoplasm where it is translated into the OEC, which, in turn, is transported to the nucleus and binds to the targeted EpiZip within the specified IGD. We are currently exploring a range of cationic and ionizable LNPs from various internal and external sources and have developed proprietary LNP formulations that have shown specific and efficient *in vivo* functional delivery in preclinical studies.

***4. Industry-Leading Computational, Biological, and Genomic Expertise***

We leverage codified learnings and insights gleaned from our lead programs to continue optimizing our platform and inform the discovery and development of subsequent product candidates. We have also established and continue to add to our knowledge bank of EpiZips and OECs. We take a rational and streamlined approach to the development of programmable epigenetic medicines to potentially provide a faster path to the clinic through robust and efficient target identification, validation, product-candidate design, and optimization. We are also continually expanding our catalog of EpiZips and novel and proprietary DNA-binding domains and epigenomic effector proteins and using computational methods to assess on-target and potential off-target binding and activity to minimize inadvertent changes in the expression of genes.

***Computational Foundation***

The OMEGA platform leverages novel biology and epigenetics to therapeutically control gene expression and program cell state through our significant computational capabilities. Decoding the rules of the human genome – one with billions of nucleotides, tens of thousands of genes, and up to a million regulatory sequences, all potentially interacting in 3-dimensional space – requires the creation of advanced proprietary algorithms and statistical data analysis techniques. Our cutting-edge computational tools are built on a diverse library of proprietary algorithms and deep-learning techniques, which enable us to interpret and predict the location, structure and function of IGDs. The critical scientific insights provided by the OMEGA platform enable the identification of EpiZips across therapeutic areas and indications. This deep *in silico* understanding and predictability also directly informs the design and rapid engineering of OECs that allow us to regulate single or multiple genes with exquisite specificity, controllable tuning, and duration of effect.

We apply our computational technology throughout the drug development continuum by broadly applying a computation- and data-first approach. We deploy a wide range of systems biology and functional genomics methods to identify relevant biomarkers. We utilize key translational models to validate mechanism of action in order to accelerate development and potentially de-risk clinical translation. Combinatorial optimization techniques and novel discovery efforts enable acceleration of delivery and formulation design. This allows us to rapidly scale programs and manufacturing while improving quality and cost. Systematic data capture and automation have enabled real-time, data-driven decision-making which has further driven our ability to accelerate numerous programs in parallel.

We have a highly skilled computational team with deep expertise and broad experience, supporting the OMEGA platform. This team develops the tools, capabilities, and specialized methods needed to address the complexity of IGD biology, design, and delivery of our OECs, and integration of a computation- and data-first philosophy company wide. We are continually growing and evolving our computational team and capabilities to drive innovation in the discovery and development of programmable epigenetic medicines, manufacturing, and our digital foundation.

## Our Development Programs

Our current pipeline consists of development programs in oncology, multigenic diseases including immunology, regenerative medicine, and select monogenic diseases.

***Oncology***

*OTX-2002 for Hepatocellular Carcinoma*

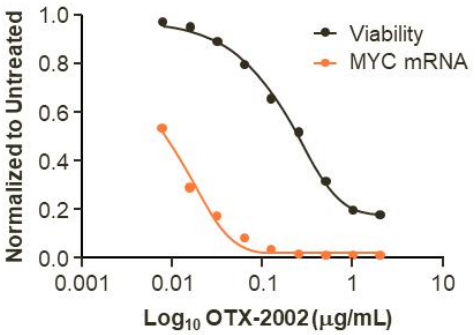
We are developing OTX-2002 to downregulate c-Myc, an oncogene that is dysregulated in more than 50% of human cancers and is frequently associated with poor prognosis, as a potential treatment for patients with advanced HCC. c-Myc has been shown to play a key role in liver cell proliferation and is known to be upregulated in the majority of HCC cases. Drug development aimed at directly targeting c-Myc has proved challenging because its expression is tightly regulated and because it is a protein that lacks a specific active site for small molecule binding. This means that targeting c-Myc mRNA or protein is unlikely to be effective as neither approach addresses the underlying dysregulation at the transcriptional level. Unlike other more binary approaches to downregulation of gene expression, OECs can precisely modulate c-Myc expression enough to kill highly MYC-amplified cancer cells and drive tumor regression, but spare healthy surrounding cells which need only a low level of MYC for normal function.

HCC is a primary liver malignant tumor that develops in a chronic-liver-disease setting. It is typically diagnosed late in its course and the median survival period following diagnosis is approximately six to 20 months. In 2017, there were an estimated 89,950 people living with liver and liver-related cancer in the United States. Depending on the stage of disease at diagnosis, current treatment options include therapies such as surgical resection, tyrosine kinase inhibitors (TKIs), such as sorafenib, orthotopic liver transplantation or radiofrequency ablation, and for more advanced patients, immune checkpoint plus anti-vascular-endothelial-growth-factor combination therapy, or palliative treatments, such as trans-catheter arterial chemo- or radio-embolization, stereotactic radiation therapy or systemic chemotherapy.

When tested in a panel of HCC cell lines, OTX-2002 made epigenetic modifications in precisely targeted regions in the chromosome, leading to a reduction in MYC mRNA levels and driving antiproliferative effects. In preclinical studies utilizing both subcutaneous and orthotopic mouse xenograft models of HCC, OTX-2002 led to significant tumor growth inhibition with no significant impact on body weight change in mice. The antitumor activity was consistent with reduction in MYC protein levels in the tumors. Further, in both in vitro and in vivo studies, OTX-2002 in combination with lenvatinib or sorafenib, the current standard of care agents in HCC, was associated with enhanced inhibition of tumor growth in HCC tumor models.

In a preclinical study of OTX-2002 in various HCC cell lines, OTX-2002 down-regulated c-Myc and we observed loss of cellular viability across targeted HCC subtypes with effects observed for 15 days. As shown in the graph below, the $EC_{50}$, which measures the concentration of a drug that provides a 50% response between baseline and the maximum response, was measured in five HCC cell lines. Treatment with OTX-2002 resulted in a c-Myc mRNA expression $EC_{50}$ at a mean value 0.013 ug/mL and a 50% decrease in cell viability at 0.147 ug/mL.

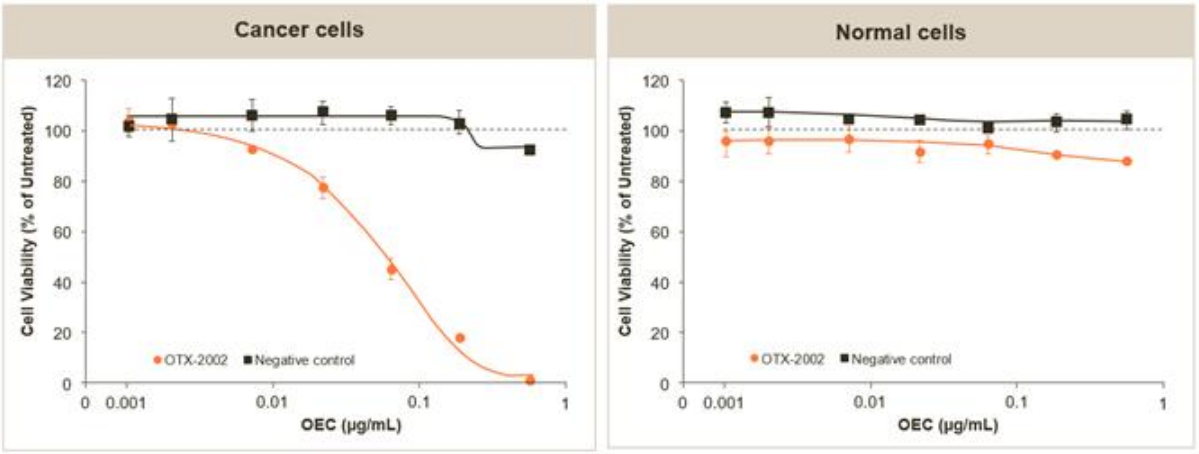
**OTX-2002 was associated with a dose-response on expression and viability *(in vitro)***




In a separate preclinical study of OTX-2002 in an HCC cell line (Hep3B), we demonstrated a selective effect on the viability of cancer cells. As shown in the graph below, treatment of cancer cells with OTX-2002 at concentrations ranging from 0.001 to 500 ng/mL resulted in a significant reduction in the viability of these cells at

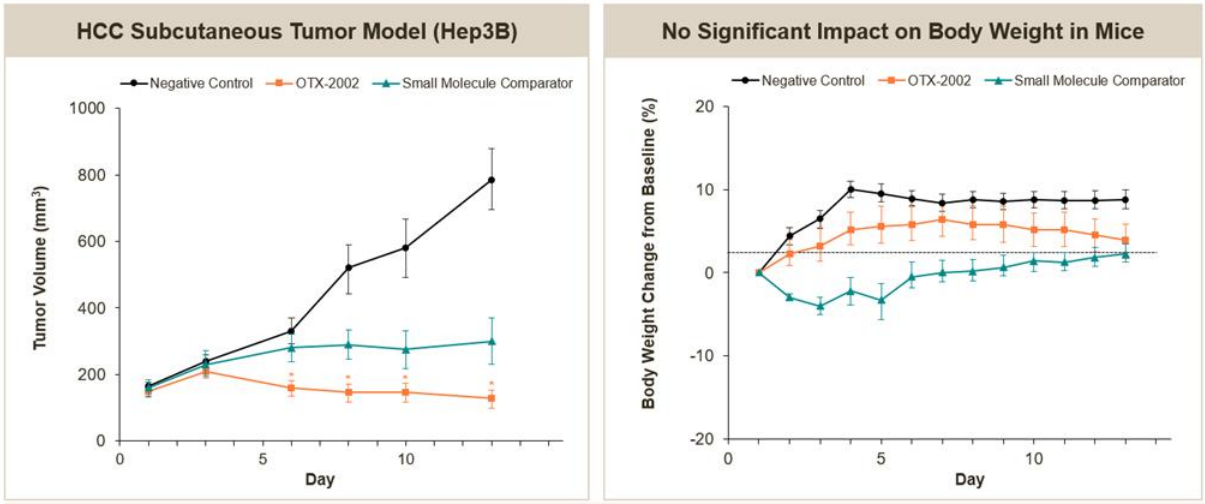
all doses, where, by contrast, when we treated normal cells (healthy primary human liver hepatocytes) with OTX-2002 we saw no significant impact on cell viability.

**OTX-2002 reduced viability of HCC cancer cells but not healthy human liver cells (*in vitro*)**




OTX-2002 delivered via formulated LNPs in vivo decreased tumor burden in mice containing human HCC xenografts. In this preclinical study, we administered 3 mg/kg OTX-2002 every five days in a mouse subcutaneous tumor model or a small molecule control. As shown in the graph below, treatment with OTX-2002 was associated with a statistically significant inhibition of tumor growth, resulting in a 78% inhibition of tumor growth by Day 13 compared to the negative control. Treatment with OTX-2002 was equivalent to treatment with the small molecule comparator. Mice treated with OTX-2002 did not experience a significant decrease in body weight. OTX-2002 was well tolerated in this study with no adverse events observed.

**OTX-2002 anti-tumor activity and dose-dependent response observed in HCC subcutaneous xenograft model, with no significant impact on body weight *(in vivo)***

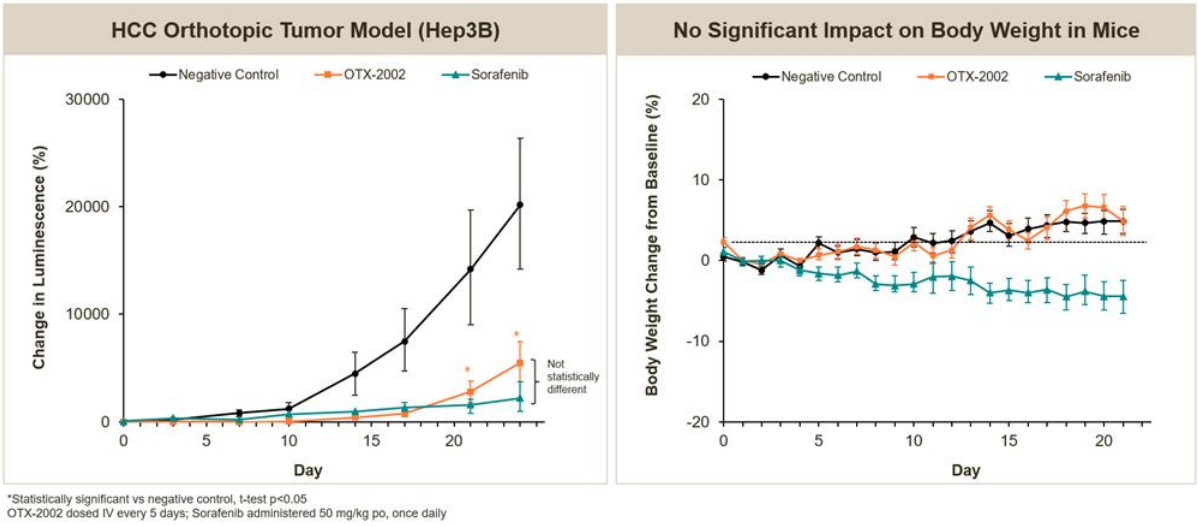



***Statistically significant vs negative control, t-test p<0.05 starting on Day 6. OTX-2002 dosed IV every 5 days***.

In addition, we observed an equivalent effect on tumor growth from OTX-2002 in mice containing human HCC xenografts compared to sorafenib. Mice were administered 3 mg/kg of OTX-2002 every five days or 50

mg/kg of sorafenib once daily. Tumor growth was measured using bioluminescent imaging. As shown in the graph below, treatment with OTX-2002 resulted in a comparable reduction in luminescence as treatment with sorafenib. Mice treated with OTX-2002 did not experience a significant decrease in body weight. Mice treated with sorafenib experienced a sustained loss in body weight. OTX-2002 was well-tolerated in this study with no adverse events observed.

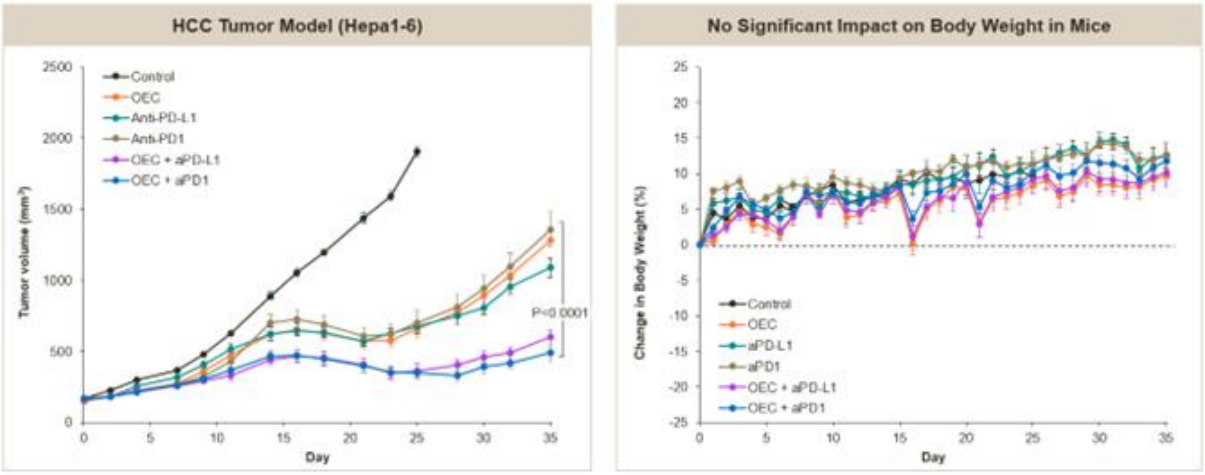
**OTX-2002 anti-tumor activity and change in body weight observed in HCC orthotopic xenograft model (in vivo*)***




*Statistically significant vs negative control, t-test p<0.05
OTX-2002 dosed IV every 5 days; Sorafenib administered 50 mg/kg po, once daily

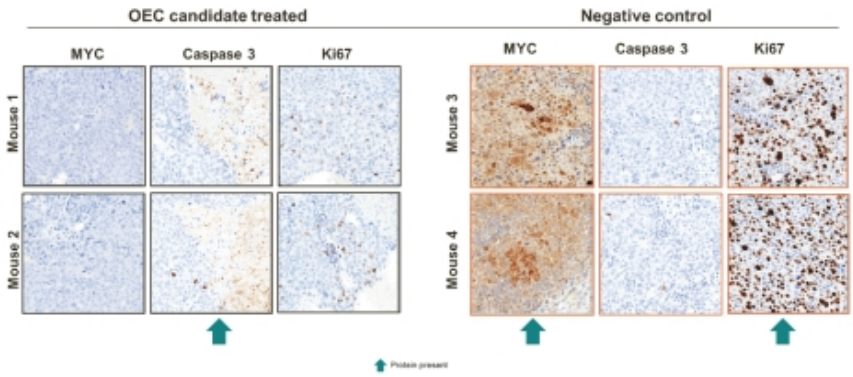
We have also observed statistically significant combination efficacy benefit with checkpoint inhibitors, including both anti-PD-1 and anti-PD-L1 agents. In evaluation of a mouse surrogate OEC for OTX-2002 in a subcutaneous HCC tumor model (Hepa1-6), groups of immune competent mice were administered 1 mg/kg of the OEC every five days, 10 mg/kg of either anti-PD1 or anti-PD-L1 weekly, combinations of the OEC and anti-PD1 or anti-PD-L1, or a negative control. As shown in the graph below, combination treatment resulted in statistically significant inhibition of tumor growth compared to the negative control, and further, statistically significant inhibition of tumor growth compared to all of the monotherapy treatment arms. Both combination arms were well tolerated with no significant impact on body weight observed during the study.

**Treatment with OEC in combination with anti-PD1 or anti-PDL1 anti-tumor activity and body weight observed in HCC xenograft model*(in vivo)***




*In vivo* treatment of OTX-2002 delivered via formulated LNPs in a mouse subcutaneous human HCC tumor model at a doses of 3 mg/kg every five days resulted in decreased tumor burden and also showed correlated changes in c-Myc expression and associated clinical biomarkers in tumors at the cellular level. As shown in the graph below, immunohistochemistry analysis of histology sections from OEC candidate-treated and negative control tumors harvested from the animals in the *in vivo* studies described above showed significant downregulation of c-Myc protein in the tumors (indicated by loss of brown staining) as well as the expected downregulation of Ki67 (a biomarker of tumor cell proliferation) and upregulation of Caspase 3 (a biomarker of apoptosis, a type of programmed cell death).

**Change in clinical biomarkers observed in HCC xenograft model**




In July 2022, we announced clearance of our investigational new drug (“IND”) application from the United States Food and Drug Administration ("FDA") to initiate a Phase 1/2, first-in-human, clinical trial of OTX-2002 for the treatment of HCC.

In October 2022, we announced initiation of the Phase 1/2 MYCHELANGELO™ I clinical trial. The study will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of OTX-2002 as a monotherapy (Part 1) and in combination with standard of care therapies (Part 2) 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 up to 190 patients at clinical trial sites in the United States, Asia, and Europe.

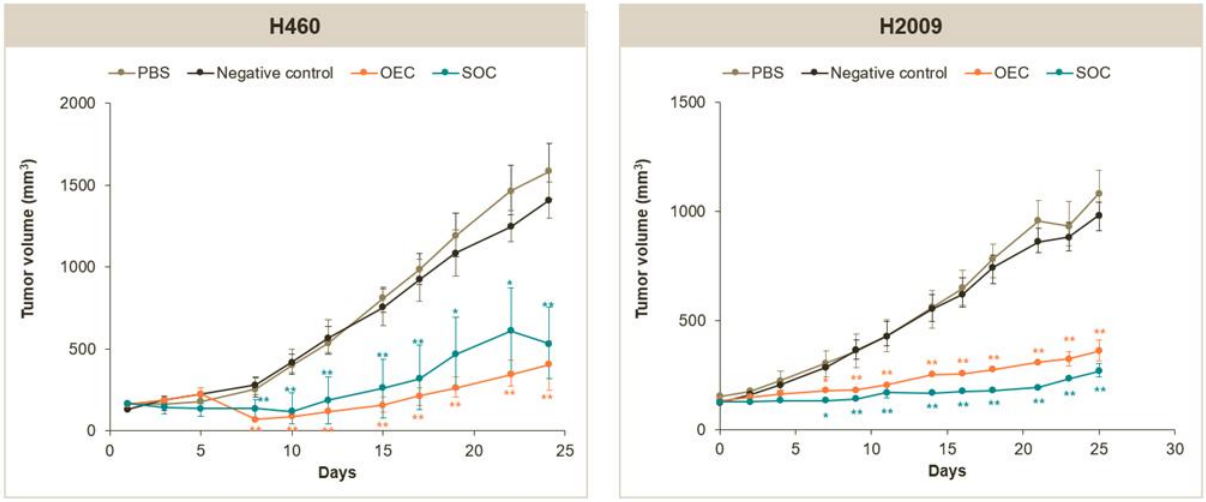
In November 2022, we announced that OTX-2002 was granted Orphan Drug Designation by the FDA for the treatment of HCC.

*OTX-2101 for Non-Small Cell Lung Cancer*

In October 2022, we announced the selection of OTX-2101 as a development candidate to advance into IND-enabling studies for the treatment of NSCLC. Approximately 50% of NSCLC tumors overexpress c-Myc. We are developing OTX-2101 to downregulate c-Myc and reduce this overexpression. NSCLC is the most common type of lung cancer, accounting for 84% of all lung cancer diagnoses, which was approximately 192,200 new cases in the United States in 2020. The five-year survival rate for NSCLC is 24%. Depending on the stage of disease at diagnosis, current treatment options include therapies such as surgical resection, photodynamic therapy (PDT), laser therapy, or brachytherapy, chemotherapy, radiation therapy, targeted therapies (e.g., TKIs) and immunotherapy in combination with other therapies.

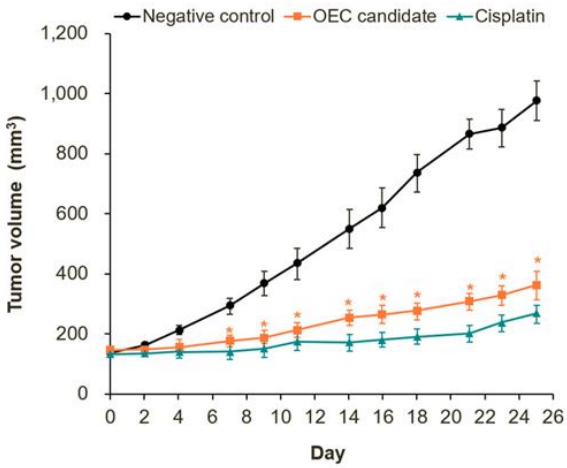
We have identified OEC candidates that have shown activity against a range of NSCLC cell lines in vitro in preclinical studies, showing down-regulation of c-Myc with concomitant loss of cellular viability. Importantly, in in vitro preclinical studies, minimal antiproliferative effects in normal primary lung epithelial cells, fibroblasts, and endothelial cells were observed with these OEC candidates. In addition, the OEC candidates showed synergistic effects on cell proliferation in a preclinical study when treated in combination with clinically relevant TKIs (data not shown). We also conducted preclinical studies in two subcutaneous xenograft models of NSCLC. In these studies, we treated mice with 3 mg/kg of one of our OEC candidates every five days. Treatment with our OEC candidate showed a statistically significant reduction in tumor size during the dosing phase of the study, with no reduction in body weight of treated mice observed. In these two studies, treatment with our OEC candidate was associated with an equivalent effect on tumor volume to treatment with the standards of care, chemotherapy medication used to treat several cancers, as shown in the graphs below.

**OEC candidate anti-tumor activity in H460 and H2009 NSCLC subcutaneous xenograft models *(in vivo)***



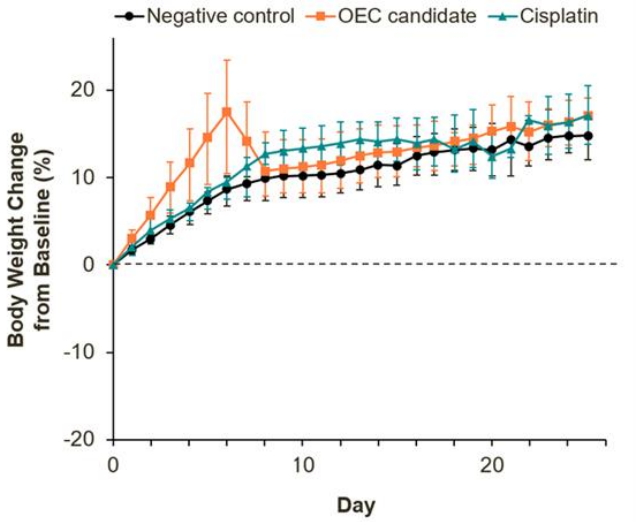

**p<0.01, *p<0.05

**Anti-tumor activity observed in NSCLC subcutaneous xenograft model *(in vivo)***




**** p<0.05 compared to negative control***

**Change in body weight observed in NSCLC subcutaneous xenograft model (*in vivo*)**




In a panel of NSCLC cell lines, OTX-2101 reduced viability and induced apoptosis, consistent with reduction in MYC mRNA levels. Further analysis of the OTX-2101-treated cells showed specific binding of the mRNA drug substance to its predicted genomic target region and an increase in the expected epigenetic mark(s) at the target site. In preclinical studies in subcutaneous xenograft models of NSCLC, we observed significant inhibition of tumor growth at well tolerated doses of OTX-2101. OTX-2101 showed combination benefit in NSCLC cells in vitro, when treated either with MEK inhibitor (trametinib), or EGFR inhibitor (Osimertinib), which we believe demonstrates OTX-2101's potential to offer a potential differentiated treatment modality in advanced NSCLC.

*Small Cell Lung Cancer*

We are also targeting SCLC through epigenetic control points that down-regulate a gene known to be overexpressed in more than 90% of SCLC due to a common mutation, and also overexpressed in other cancers including breast, lung, acute myeloid leukemia, and gastric cancers. This gene is located in an identified and well-characterized single-gene IGD. SCLC accounts for 15% of all lung cancers and has a five-year survival rate of

6%. Depending on the stage of disease at diagnosis, current treatment options include surgical resection followed by chemotherapy, chemotherapy with radiation, and immunotherapy.

We conducted proprietary algorithmic analysis of the IGD, using a wide range of multi-omic datasets, to identify numerous EpiZip targets and epigenomic effector options. We are generating computationally designed OEC candidates using our OMEGA platform for the potential treatment of SCLC and conducting *in vitro* testing to determine the final OEC candidate for *in vivo* testing.

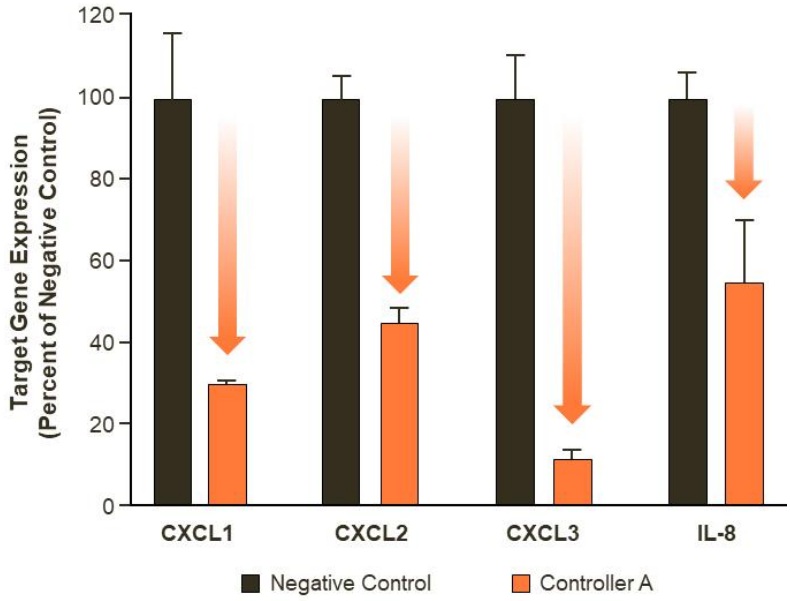
***Multigenic Diseases Including Immunology***

*Acute Respiratory Distress Syndrome (ARDS)*

We are evaluating OEC candidates to reduce expression of the CXCL1, 2, and 3 and IL-8 gene cluster in various potential indications, including inflammatory lung diseases such as neutrophilic asthma and ARDS, dermatological and rheumatological indications, and oncology. Overexpression of the CXCL gene cluster produces chemokines that attract neutrophils and promotes local inflammation. In the case of ARDS, chemokines that recruit inflammatory cells to the lung are of pivotal importance in disease pathogenesis and expression of the CXCL1, 2, 3, and IL-8 gene cluster is elevated in the lung cells of patients with ARDS. ARDS is a devastating syndrome, with an incidence of approximately 200,000 in the United States and a mortality rate approaching 40%.

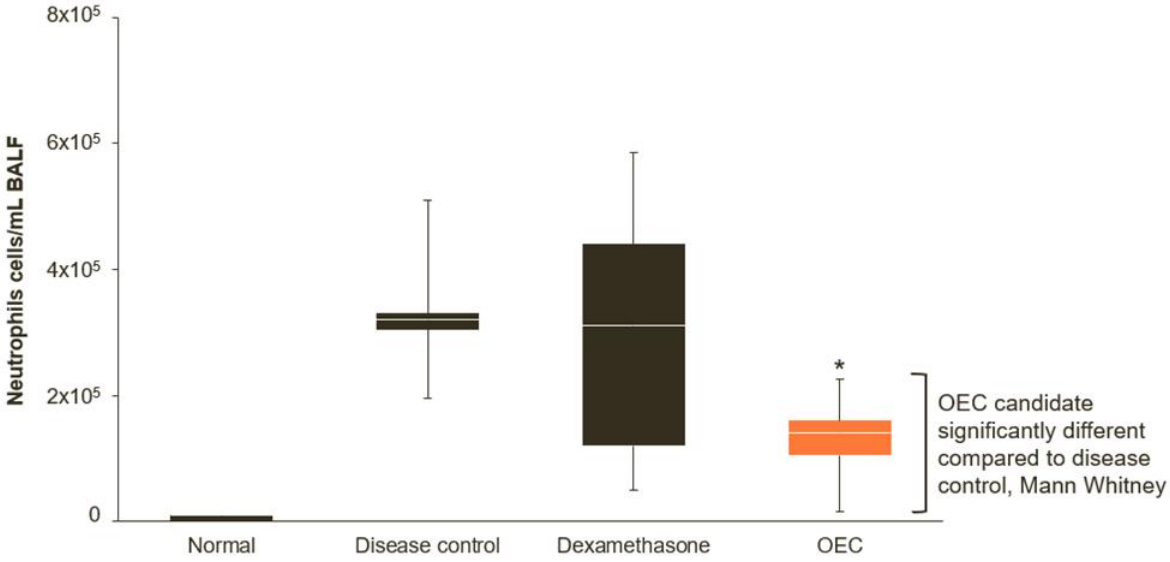
In a preclinical study of an OEC candidate (Controller A in the graph below) in human monocytes, at 24 hours post-dosing we observed a 65% decrease in gene expression of CXCL1, a 55% decrease in gene expression of CXCL2, an 88% decrease in gene expression of CXCL3, and a 52% decrease in gene expression in IL-8, in each case relative to control.

**Multigenic IGD targeting of chemokine genes observed *(in vitro)***




In a preclinical study in an animal model of ARDS, we observed a significant decrease in neutrophil infiltration in lungs treated with an OEC candidate. Animals were administered 3 mg/kg of the OEC candidate two hours prior and eight hours after lipopolysaccharide insult to induce inflammation or 10 mg/kg dexamethasone daily as a positive control. As shown in the graph below, we observed a 56% decrease in neutrophils infiltration in broncho-alveolar lavage fluid (labeled BALF in the graph below) in mice 72 hours after treatment with the OEC candidate relative to disease control, a measure of the severity of the inflammatory response.

**Decreased neutrophil infiltration in ARDS model (*in vivo*)**




**** p<0.05 compared to disease control***

We also plan to conduct *in vivo* testing in other models of severe inflammatory disease where the CXCL1, 2 and 3 and IL-8 gene cluster plays a key role, such as neutrophilic dermatosis, paw edema, and rheumatoid arthritis.

*Idiopathic Pulmonary Fibrosis*

We are evaluating OEC candidates to down-regulate expression of a gene cluster known to be up-regulated in patients with idiopathic pulmonary fibrosis, or IPF, and promote pulmonary fibrosis in animal models. IPF is a rapidly progressive and fatal disease in which the lung loses its functional capacity over time. The global prevalence for IPF is roughly 13 to 20 per 100,000 persons, and there is no known cure. The average patient survival is approximately six years with treatment and three years without treatment. Current treatment options are limited to symptomatic or palliative care, including anti-fibrotics, anti-inflammatories, corticosteroids, oxygen therapy, and for advanced disease, lung transplant. If we are able to successfully down-regulate expression of this gene cluster in human lung cells, we believe this OEC candidate could also be developed for severe chronic obstructive pulmonary disease and asthma, as the same gene cluster is implicated in these indications as well as in IPF.

We have conducted algorithmic analysis, using a wide range of multi-omic datasets, to identify an IGD with an internal structure consisting of seven genes related to IPF controlled through various intra-IGD interactions and regulatory elements. We are generating computationally designed OEC candidates using our OMEGA platform for the potential treatment of IPF and conducting *in vitro* testing to determine the final OEC candidate for *in vivo* testing.

***Regenerative Medicine***

*Liver Regeneration*

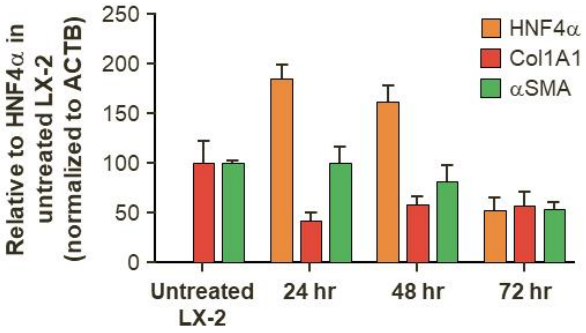
We are developing OEC candidates designed to increase expression of HNF4 , a transcriptional master regulator, as a potential way to restore liver-cell function in patients with severe liver dysfunction. HNF4 controls development, differentiation, and homeostasis of hepatocytes and other cell types in the liver by controlling the expression of proteins, such as bilirubin, albumin, and metabolic enzymes, which are essential for normal liver

function. In chronic liver disease, HNF4 is down-regulated, which contributes to the pathology of liver failure. Studies have shown that increased expression of HNF4 in even a modest fraction of hepatocytes can restore healthy liver function.

In 2020, chronic liver disease and cirrhosis were a leading cause of death in the United States, accounting for over 50,000 deaths. Depending on the etiology of disease, treatment options may include corticosteroids, antivirals or other drugs, with the final option being liver transplantation. In 2018, in the United States, there were more than 14,000 people on the liver transplant waiting list and approximately 25% died before receiving a transplant.

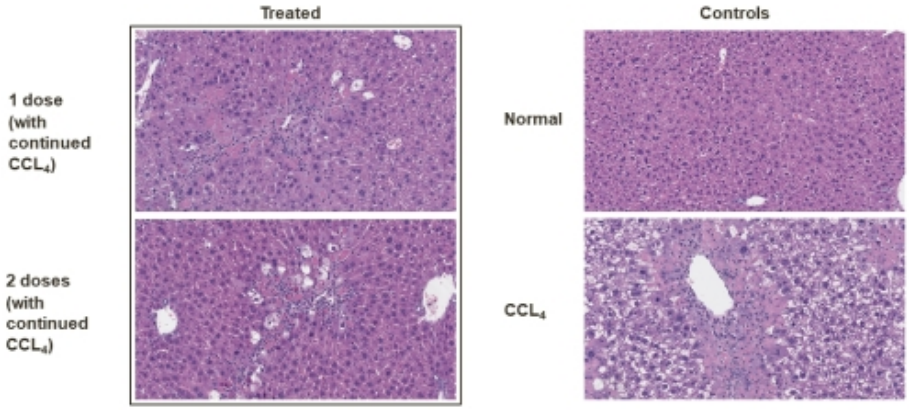
In preclinical studies in primary healthy human hepatocytes, treatment with our OEC candidate induced a durable increase in HNF4 for up to ten days, which we believe may be sufficient to return hepatocytes to a functional state and restore liver function in CLD and ESLD patients. We also observed decreases in collagen 1A1, or Col1A1, and alpha smooth muscle actin, or SMA, both biomarkers of liver injury and fibrosis, as shown in the graph below. At 72 hours, we observed reductions of approximately 50% in both Col1A1 and SMA relative to untreated cells. These data showed a reduction in expression of these downstream biomarkers of liver damage in response to the up-regulation of HNF4 and support the proposed therapeutic mechanism of action of our OEC candidate.

**OEC candidate reduced biomarkers of liver damage (*in vitro*)**




As shown in the images below, in an *in vivo* preclinical mouse liver fibrosis model, carbon tetrachloride treatment was used to induce hepatocellular degeneration (labeled $CCL_4$ in the images below). Treatment with a mouse surrogate construct of our OEC candidate showed a significant decrease in hepatocellular degeneration on Days 31 and 38 with either one or two weekly administrations.

**Mouse surrogate construct of OEC candidate improved liver histology (*in vivo*)**



We are currently conducting additional *in vitro* and *in vivo* pharmacology, formulation optimization, efficacy, and preliminary safety studies of our OEC candidate.

*Corneal Regeneration*

We are also evaluating OEC candidates to control the expression of multiple potential target genes in patients with diabetes and other conditions to treat corneal epithelial injury. The proteins expressed by these genes have been strongly linked to cell-growth inhibition and shown to be key factors in preventing ocular wound-healing in animal models. Approximately 70% of patients with diabetes suffer from corneal complications, including epithelial fragility, recurrent erosions, ulcers, and delayed or incomplete wound repair. Diabetic retinopathy is currently the leading cause of legal blindness in working age adults worldwide. The condition is mainly treated by attempting to maintain tight blood glucose control. We believe that by tuning these genes, we may be able to facilitate corneal regeneration to treat these corneal complications from diabetes or other conditions.

We have identified an IGD containing a master regulatory gene that has been strongly linked to cell-growth inhibition in patients with diabetes and other conditions. We conducted algorithmic analysis of the IGD, using a wide range of multi-omic datasets, to identify numerous EpiZip targets and epigenomic effector options. Using our OMEGA platform, we are generating computationally designed OEC candidates for the potential treatment of corneal generation and conducting *in vitro* testing to determine the final OEC candidate for *in vivo* testing.

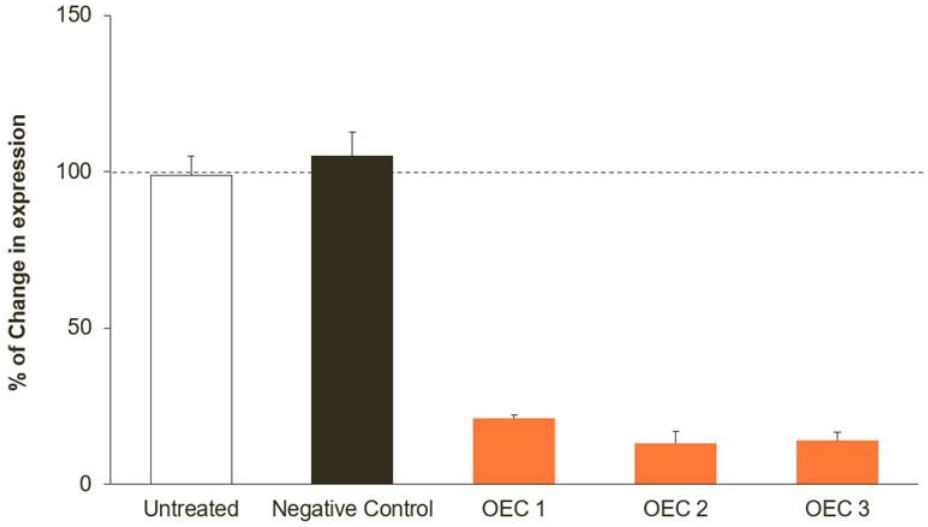
***Select Monogenic Diseases***

*Alopecia*

We are developing OEC candidates for the treatment of alopecia, a disorder characterized by patches of non-scarring hair loss affecting the scalp and body. We are targeting SFRP1, a protein that inhibits hair growth in alopecia patients, and are developing OEC candidates designed to down-regulate the production of SFRP1. Alopecia areata affects approximately 6.5 million people in the United States and approximately 2% of people worldwide. Androgenetic alopecia, also known as male pattern baldness, is a genetically predetermined disorder caused by excessive response to androgens, which affects up to 50% of males and females. There is currently no cure for either type of alopecia. We are evaluating delivery of our OEC candidates to the hair bulb and assessing our OEC candidates' effects in *ex vivo* models of hair growth.

In a preclinical study, we treated patient human papilla cells with an OEC candidate and measured SFRP1 mRNA expression. As shown in the figure below, we observed a 79% to 88% reduction in SFRP1 mRNA expression in cells treated with the OEC candidate compared to control. These effects were observed through Day 7.

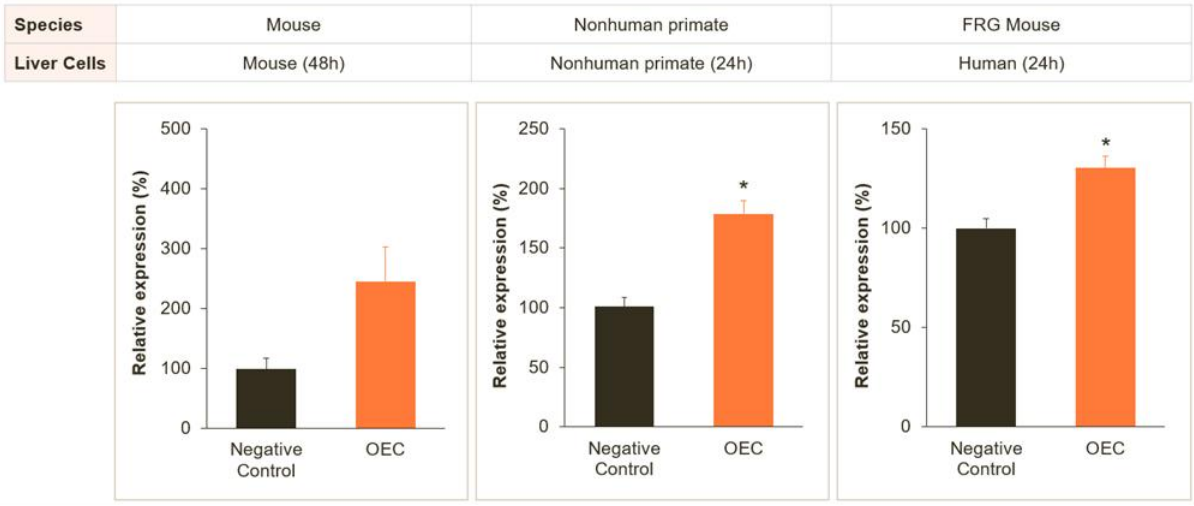
**Decrease in SFRP1 mRNA expression in human papilla cells (*in vitro*)**




***Translational Data***

A critical element for the clinical translation of our OEC candidates is our ability to design OEC candidates that can target IGDs and tune gene expression across species. In preclinical studies, we evaluated changes in HNF4 expression in non-human primates and in human liver tissue engrafted and grown in a mouse (labeled FRG Mouse in the graph below) treated with our OEC candidate and in healthy mice treated with an OEC candidate designed to target the homologous murine target sequence. As shown in the graph below, we observed therapeutically relevant up-regulation of HNF4 compared to control, with results showing a 246% increase in mice, 68% increase in non-human primates, and 31% increase in the FRG mouse. We believe that this translational fidelity of our mechanism of action supports our continued development of our OEC candidates and programs.

**Omega Epigenomic Controllers increased HNF4A expression in preclinical studies (*in vivo*)**

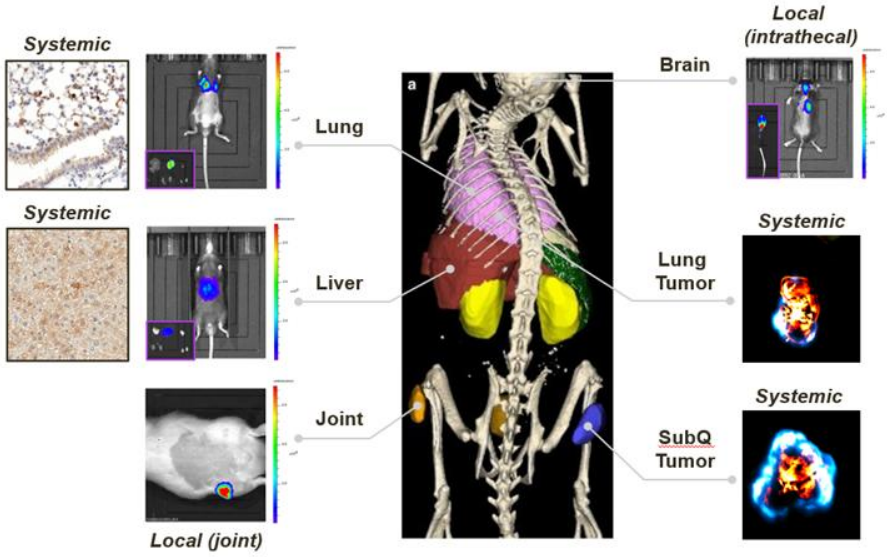



**** p<0.05 compared to negative control***

***Delivery Data***

We have extensive internal formulation, delivery and development expertise in mRNA and LNPs, and are engaged in continuous internal LNP research and development. We are currently exploring a range of LNPs from various internal and external sources and have developed proprietary formulations that have shown specific and efficient *in vivo* functional delivery of our OEC candidates to a number of therapeutically relevant cell and tissue-types in preclinical studies, as shown in the figure below. The tissue and cell types we can access with our current library of LNP compositions include liver (e.g. hepatocytes, stellate cells, Kupffer cells), lung (e.g. endothelial, alveolar, epithelial), local joints (e.g. synovial layer, chondrocytes, immune cells), and the central nervous system (e.g. spinal cord, brain), as well as tumors (e.g. subcutaneous, orthotopic). Collectively, our current delivery capabilities enable us to develop and expand our pipeline.

**Delivery of Omega Epigenomic Controllers**




**Manufacturing**

We view the development of manufacturing capability, capacity, and control as critical to our overall success and specifically to our ability to meet our development timelines, contain operational costs and generate and protect intellectual property for our platform technology and product candidates. Because of this, we have chosen a clinically validated manufacturing and delivery technology with which we have deep internal expertise and which is similar to that being developed for various applications in the fields of vaccine development and gene editing. We are thus able to leverage our own experience, as well as the technological improvements and regulatory precedents established by previous and current products utilizing the same modalities.

Our internal process and analytical development organization has established manufacturing processes at sufficient scale to supply our research and early preclinical development requirements for drug substance and drug product. In addition, we have engaged highly skilled third-party contract development and manufacturing organizations, or CDMOs, with extensive experience in manufacturing mRNA, our drug substance, and drug product to implement our manufacturing processes at large scale under current good manufacturing practices, or cGMP. We have established manufacturing services agreement with third-party CDMOs for the supply of drug substance and drug product to meet our needs for preclinical studies, IND-enabling toxicology studies and clinical trials. We expect to continue to rely on third-party CDMOs for the supply of drug substance, drug product and finished product for the next several years.

For each of our therapeutic programs, we evaluate the optimal LNP delivery options from both external collaborations and our internal LNP research and development platform. For example, for our lead program, OTX-2002, we have licensed LNP technology from Acuitas Therapeutics, Inc., or Acuitas, a company with extensive LNP intellectual property and a track record of collaborating and developing LNPs for clinical use. We believe our collaborations with external partners will provide significant formulation and manufacturing expertise that will facilitate the transfer of processes for LNP formulation of mRNA under cGMP standards to CDMOs. We are also in the process of engaging additional highly experienced CDMOs to manufacture our product candidates.

We believe that we have sufficient manufacturing capacity through our third-party CDMOs and current internal facilities to meet our current research, preclinical, and clinical material needs. We believe that the current manufacturing capacity established externally, together with the internal capacity will be sufficient to meet our anticipated needs for the next several years. We monitor the capacity availability for the manufacture of drug substance and drug product and believe that our supply agreements with our CDMOs and the lead times for new material supply would allow us to access additional capacity to meet our anticipated needs. We also believe that our product can be manufactured at a scale and with production and procurement efficiencies that will result in commercially competitive costs.

**Competition**

As an early-stage biotechnology company, we face competition from a wide array of companies in the pharmaceutical and biotechnology industries. This competition includes both small companies and large companies with greater financial and technical resources and longer operating histories than our own. We also compete with the intellectual property, technology, and product development efforts of academic, governmental, and private research institutions.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly if they establish collaborative arrangements with large companies.

The key competitive factors affecting the success of any products that we develop, if approved, are likely to be their efficacy, safety, convenience, price, and the availability of reimbursement from government and other third-party payors. Our commercial opportunity for any of our product candidates could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may commercialize products more quickly than we do.

We expect to compete with companies developing technologies that focus on gene-expression control using various technologies, such as CRISPR gene editing, gene therapies, non-coding RNA therapeutics, and small molecule epigenetics. These companies include: Alnylam Pharmaceuticals, Inc., Beam Therapeutics Inc., Biogen Inc., CRISPR Therapeutics AG, Editas Medicine Inc., Ionis Pharmaceuticals, Inc., Intellia Therapeutics, Inc., Janssen Pharmaceuticals, Inc., Pfizer Inc., and Sangamo Therapeutics Inc.

Further, while we are not aware of other companies developing epigenomic controllers and modulating gene-expression pre-transcriptionally for the treatment of either HCC or NSCLC, several companies are developing therapeutics that use gene-expression control for the treatment of HCC or NSCLC, including Ionis Pharmaceuticals, Inc., AstraZeneca plc, Alnylam Pharmaceuticals, Inc. / Ascletis Pharma Inc. and Bio-Path Holdings, Inc., which are developing anti-sense inhibitors, Nitto Denko Corporation and Simaomics, Inc., which are developing siRNA inhibitors, InteRNA Technologies B.V. which is developing micro-RNA mimic therapies, Momotaro-Gene Inc. and Genprex, Inc., which are developing gene therapy approaches, and MiNA Therapeutics Limited, which is developing a small activating RNA therapy.

These technologies, along with other modalities, such as small molecules and biologics, may be used to develop therapeutic candidates that would compete against our current, and potentially future, product

candidates. In addition, we expect any OECs we develop to compete with established therapeutic treatments, if any, in their target indication.

## Intellectual Property

We believe our intellectual property estate is a strategic asset that has the potential to provide us with a competitive advantage. We strive to protect our proprietary technology, inventions and improvements that are commercially important to our business, including pursuing, maintaining, defending, and asserting patent rights, whether developed internally or licensed from third parties. Our policy and practice is to protect our proprietary position by various methods, including filing patent applications in the United States and in jurisdictions outside of the United States related to our proprietary technology (e.g., OMEGA platform, OECs, delivery and manufacturing technology), inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates. We continue to innovate and pursue in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of epigenetic medicine. We additionally rely on data exclusivity, market exclusivity and patent term extensions when available and plan to seek and rely on regulatory protection afforded through orphan drug designations for our therapeutic products. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned by third parties; to defend and enforce our proprietary rights, including our patents; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

Our wholly owned and in-licensed patent portfolio cover various aspects of the OMEGA platform, including, manufacturing, delivery, OECs and our therapeutic programs. Our patent portfolio also covers our product candidates that are in development. As of December 31, 2022, our patent portfolio consists of 28 patent families, including 40 pending U.S. patent applications (including provisional applications), 90 pending foreign patent applications in Europe, Australia, Canada, China, Hong Kong, Mexico, and Japan, and nine owned or in-licensed Patent Cooperation Treaty (PCT) applications that have not entered national phase. Any US or foreign patents issuing from or claiming priority to the patent applications in our patent portfolio will expire between 2036 and 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees. Our objective is to continue to expand our patent portfolio to protect our proprietary technology (including the OMEGA platform, OECs, delivery and manufacturing technology), inventions, improvements and current and future product candidates. Our patent portfolio currently does not include any granted patent covering any of our product candidates.

Further details of the products and technology areas covered by our intellectual property portfolio are described below.

### OMEGA platform-related intellectual property

Our intellectual property portfolio includes know-how and patent rights directed to the OMEGA platform and delivery technology developed internally and in-licensed exclusively or co-exclusively from the Whitehead Institute for Biomedical Research, or WIBR, and Flagship Pioneering Innovations V., Inc., or Flagship.

The intellectual property portfolio for our OMEGA platform technology includes patent rights directed to compositions and methods of using OECs; methods and compositions for upregulating or downregulating gene expression by targeting IGDs; compositions for modulating gene expression by targeting IGDs with epigenetic effectors, physical disruptors and genetic modifiers; and methods for identifying and interrogating IGDs. The portfolio relates broadly to our existing product candidates and those we may develop in the future and the indications we target or may target in the future. Intellectual property related to our OMEGA platform includes a patent application owned by us. As of December 31, 2022, we owned one provisional U.S. patent application related to the OMEGA platform. We also in-license the patents and patent applications related to our OMEGA platform from WIBR and from Flagship. As of December 31, 2022, we in-licensed three issued U.S. patents, 14 non-provisional U.S. patent applications and one provisional U.S. patent application; two PCT patent applications; and 28 foreign patent applications in Europe, Australia, Canada, China, Hong Kong, Japan, Mexico, and Taiwan related to the OMEGA platform. We expect patents issuing from or claiming priority to these pending applications, if any, to expire between 2036 and 2043, excluding any patent term adjustments or extensions. The foregoing

account of our patent rights does not include rights to patents and patent applications owned by Acuitas and in-licensed to Omega pursuant to a non-exclusive license agreement or those owned by Nitto Denko Corporation, or Nitto, and in-licensed to us pursuant to an exclusive license agreement limited to a jointly developed drug candidate.

The patent portfolio for our delivery technology includes patent applications directed to LNP formulations, lipid molecules, and cell penetrating polypeptide compositions and their uses. We own certain of the patent applications related to our delivery technology and in-license certain of the patent applications from Flagship. As of December 31, 2022, we owned ten provisional U.S. patent applications and two PCT patent applications related to delivery technology. As of December 31, 2022, we also in-licensed from Flagship one issued U.S. patent and one non-provisional U.S. patent application related to delivery technology. We expect patents issuing from or claiming priority to these pending applications, if any, to expire between 2037 and 2043, excluding any patent term adjustments or extensions.

**Disease-related intellectual property**

The disease-related patent rights in our intellectual property portfolio provide coverage for OECs that specifically address certain conditions and the associated disease states. The disease-related patent applications for our lead programs include those described below. Each of the disease-related patent applications described below is either wholly owned by us or is exclusively or co-exclusively licensed from WIBR or Flagship.

***MYC***

Our OTX-2002 program targets the c-Myc family oncogene. We have developed OECs that downregulate c-Myc for the treatment of HCC. We also have a program designed to reduce the expression of c-Myc to treat NSCLC. As of December 31, 2022, we owned two provisional U.S. patent applications related to OEC compositions of matter, methods of treating c-Myc related cancers and methods of modulating c-Myc expression. As of December 31, 2022, we also in-licensed from Flagship five provisional U.S. patent applications, one foreign patent application in Taiwan and one PCT application related to OEC compositions of matter, methods of treating c-Myc related cancers and methods of modulating c-Myc expression. We expect patents issuing from or claiming priority to these pending patent applications, if any, to expire between 2037 and 2043, excluding any patent term adjustments or extensions.

***CXCL1, 2, 3, and IL-8***

We are developing OEC candidates to reduce expression of the CXCL1, 2, 3, and IL-8 gene cluster. The program is designed to reduce expression of chemokines that are over-expressed in a broad range of inflammatory disorders, including rheumatoid arthritis, gout, neutrophilic asthma, and ARDS. As of December 31, 2022, we in-licensed from Flagship two provisional U.S. patent applications relating to OEC compositions that target the CXCL 1-3/IL-8 IGD, and methods of treating inflammatory disorders, including rheumatoid arthritis. We expect patents claiming priority to these pending patent applications, if any, to expire in 2043, excluding any patent term adjustments or extensions.

***HNF4***a

Our liver regeneration program targets the master transcriptional regulator HNF4a. We have developed OEC candidates that increase expression of HNF4a to restore liver-cell function in patients with severe liver dysfunction. As of December 31, 2022, we owned one U.S. non-provisional patent application and five foreign patent applications in Australia, Canada, China, Europe, and Japan related to OEC compositions of matter and methods of treating liver disease. We expect patents issuing from these pending patent applications, if any, to expire in 2040, excluding any patent term adjustments or extensions.

***Other Disease Areas***

In addition to our disease programs listed above, we also have patent applications relating to novel OEC compositions and their use for treating additional disorders that would benefit from upregulation or downregulation of gene expression. As of December 31, 2022, we owned one PCT patent application directed to compositions

and methods of treatments for neurological disorders. We expect patents issuing from or claiming priority to these pending applications, if any, to expire between 2040 and 2042, excluding any patent term adjustments or extensions. As of December 31, 2022, we owned one non-provisional U.S. patent application and five foreign patent applications in Australia, Canada, China, Europe, and Japan directed to compositions and methods of treatment for metabolic disorder. We expect patents claiming priority to this pending application, if at all, to expire in 2040, excluding any patent term adjustments or extensions. As of December 31, 2022, we in-licensed from WIBR and Flagship two U.S. non-provisional patent applications and one PCT patent application directed to compositions and methods of treatment for cancer. We expect any patents issuing from these pending applications, if any, to expire between 2036 and 2039, excluding any patent term adjustments or extensions. As of December 31, 2022, we owned one non-provisional U.S. patent application and five foreign patent applications in Australia, Canada, China, Europe, and Japan directed to compositions and methods of treatment for inflammatory disorders. We expect patents claiming priority to these pending applications, if at all, to expire in 2041, excluding any patent term adjustments or extensions. As of December 31, 2022, we owned one PCT patent application directed to compositions and methods of treatments for alopecia. We expect patents issuing from or claiming priority to this pending application, if any, to expire in 2042, excluding any patent term adjustments or extensions.

We intend to continually assess and refine our intellectual property strategy and file additional patent applications as we develop new platform technologies and product candidates.

**License Agreements**

We are a party to license agreements under which we license patents, patent applications, and other intellectual property from third parties. The licensed intellectual property covers, at least in part, methods and compositions for regulating gene expression by targeting IGDs. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

***License Agreement with Flagship***

In March 2019, we entered into an agreement, or the Flagship Agreement, with Flagship, pursuant to which we (i) irrevocably and unconditionally assigned to Flagship all of our right, title and interest in and to certain foundational intellectual property conceived prior to the "Launch of the Company", which is defined as the earlier of our closing of the Series B financing or the first day of employment by our CEO (such foundational intellectual property, the Foundational IP) and (ii) obtained an exclusive, worldwide, royalty-bearing, sublicensable, transferable license from Flagship under such Foundational IP to develop, manufacture and commercialize any product or process or component thereof, the development, manufacturing and commercialization of which would infringe at least one valid claim of Foundational IP absent the license granted under the Flagship Agreement in the field of therapeutics during the term of the Flagship Agreement. In addition, Flagship irrevocably and unconditionally assigned to us all of its right, title and interest in and to any and all patents claiming any inventions conceived (i) solely by Flagship Pioneering, Inc., or Flagship Management, or jointly by Flagship Management and us, (ii) after the "Launch of the Company", and (iii) as a result of activities conducted pursuant to that certain managerial agreement with Flagship Management, or the Managerial Agreement, or other participation of Flagship Management in our affairs, but excluding Foundational IP. Foundational IP is directed, among other things, to the OMEGA platform, including to general methods and compositions (OECs) to modulate gene expression by targeting IGDs and specific compositions and methods directed to specific targets for the treatment of various disorders, such as MYC and CXCL1, 2, 3 & IL-8 related disorders. We utilize the rights granted by Flagship under the Flagship Agreement in our OMEGA platform and our therapeutic product candidates, including our therapeutic programs directed to MYC and CXCL1, 2, 3 & IL-8 programs. As of December 31, 2022, the Foundational IP was expected to expire between 2037 and 2042. The license granted to Foundational IP is contingent upon our compliance with our obligations under the Flagship Agreement. Our obligations under the Flagship Agreement include the use of commercially reasonable efforts to develop and commercialize licensed products and payments required under the Flagship Agreement, including royalties on net sales of the licensed products. Pursuant to the Flagship Agreement, we are obligated to pay Flagship, on a licensed product-by-licensed product and jurisdiction-by-jurisdiction basis, royalties in the low single-digit percentage on net sales of licensed products. We are solely responsible for the clinical development of any product candidates we develop based on the Foundational IP. Under the Flagship Agreement, Flagship retains the right to practice Foundational

IP within the field of therapeutics solely for non-commercial research and development purposes and to perform its duties under the Managerial Agreement.

The Flagship Agreement will terminate on the last to expire royalty term, which will expire, on a licensed product-by-licensed product and jurisdiction-by-jurisdiction basis, upon the expiration of the last valid claim of any Foundational IP covering such licensed product. Upon expiration of the royalty term with respect to a licensed product in any jurisdiction and payment in full of all amounts owed under the Flagship Agreement for such licensed product, the license granted to us will automatically convert into a non-exclusive, fully paid up license for such licensed product in such jurisdiction. We have the right to terminate the Flagship Agreement in its entirety for convenience upon 60 days of written notice. Either party may terminate the Flagship Agreement upon a material breach by the other party that is not cured within 30 days after receiving written notice. Also, Flagship may terminate (i) upon 30 days' written notice if we cease to carry on our business with respect to the rights granted in the Flagship Agreement, (ii) upon written notice if we experience an event of bankruptcy, or (iii) immediately upon written notice if we challenge the validity, patentability, or enforceability of any Foundational IP or participate in any such challenge. If Flagship determines that we have not used commercially reasonable efforts to develop and commercialize a licensed product in a specific sub-field within the licensed field, Flagship has the right to terminate the license, on prior written notice, with respect to such licensed product in such sub-field. However, in such event, we may retain our license with respect to such licensed product and sub-field if Flagship approves a written plan for development and commercialization.

***Exclusive and Co-Exclusive License Agreements with WIBR***

In May 2019, we and WIBR entered into an exclusive license agreement, or the WIBR Exclusive Agreement. Under the WIBR Exclusive Agreement, we received an exclusive, worldwide, royalty-bearing, sublicensable license under certain patent rights owned or controlled by WIBR to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes in the field of human and animal therapeutics and diagnostics. The licensed patents under the WIBR Exclusive Agreement are directed to, among other things, methods and compositions for modulating gene expression in IGDs.

In May 2019, we also entered into a co-exclusive license agreement with WIBR, or the WIBR Co-Exclusive Agreement. Under the WIBR Co-Exclusive Agreement, we received a co-exclusive, worldwide, royalty-bearing, sublicensable license under certain patent rights owned or controlled by WIBR to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes in the field of human and animal therapeutics and diagnostics. Our co-exclusive rights under the WIBR Co-Exclusive Agreement will become exclusive if the co-exclusive license agreement between WIBR and the co-exclusive licensee is terminated at any time for any reason. The licensed patents under the WIBR Co-Exclusive Agreement are directed to, among other things, methods and compositions for modulating gene expression through targeting IGDs. The WIBR Exclusive Agreement and the WIBR Co-Exclusive Agreement are collectively referred to as the WIBR Agreements.

Under the WIBR Agreements, WIBR retains the right to practice the licensed patents for research, teaching, and other educational purposes, including use in third-party sponsored research, and to grant non-exclusive licenses to other academic and not-for-profit research institutes solely for non-commercial research, teaching, and other educational purposes.

The licenses granted to us under the WIBR Agreements are subject to certain preexisting rights held by the U.S. government. The U.S. government retains certain rights under applicable law with respect to licensed patents that arose from federal research funding. The license granted to us under the WIBR Agreements is further subject to certain preexisting rights held by a certain third party who is a party to a certain sponsored research agreement, or SRA, with WIBR. Under the SRA, WIBR covenanted not to sue said third party if certain inventions arising under the SRA, or SRA inventions, are dominated by the licensed patents and we are thereby excluded from asserting any patent rights licensed from WIBR that cover the SRA inventions against said third party. Furthermore, beginning five years after the effective date of the WIBR Exclusive Agreement, if WIBR or we receive a request from a third party for a sublicense under the licensed patent rights to make, have made, use, sell, offer to sell, or import a product or process that is not directly competitive with a licensed product or licensed process then offered for sale or in bona fide research or development by or on behalf of us, we must either (i) enter into a good faith negotiation toward granting a non-exclusive sublicense limited to the third party's proposed

field and proposed product, or (ii) at our election, submit a plan for WIBR's approval for development of the proposed product, which approval must not be unreasonably withheld.

Under the WIBR Exclusive Agreement, we are required to pay WIBR an annual license maintenance fee in the mid five figures. WIBR is also entitled to receive potential clinical and regulatory milestones up to $1.7 million in the aggregate for each of the first three licensed products (excluding backup products). During the year ended December 31, 2022, we incurred approximately $0.1 million of expenses, consisting of license maintenance fees, reimbursable patent costs and milestone payment, under the WIBR Exclusive Agreement. With respect to the sale of licensed products by us, our affiliates or our sublicensees, WIBR is entitled to receive a low single-digit percentage royalties on net sales of licensed products until, on a country-by-country basis, the expiration or abandonment of the patent rights. We are entitled to certain customary reductions and offsets on these royalties with respect to a licensed product in a given country. If we sublicense our rights to develop or commercialize a licensed product under the WIBR Exclusive Agreement, WIBR is entitled to a percentage of non-royalty payments that we receive from our sublicenses, ranging from zero to the low double-digits, depending on the stage of development our licensed products at the time such sublicense is executed.

Unless earlier terminated, the WIBR Exclusive Agreement will remain in effect until the expiration or abandonment of all licensed patent rights. We may terminate the WIBR Exclusive Agreement at our convenience following written notice to WIBR. Either party may terminate the WIBR Exclusive Agreement for an uncured material breach of the other party. WIBR may also terminate the WIBR Exclusive Agreement in the event that Omega ceases to carry on its business. The last to expire patent under the WIBR Exclusive Agreement, if issued, is expected to expire in 2038.

Under the WIBR Co-Exclusive Agreement, we are required to pay WIBR an annual license maintenance fee in the low to mid five figures. WIBR is also entitled to receive potential clinical, regulatory, and sublicensing milestones up to $1.9 million in the aggregate for each of the first three licensed products (excluding backup products). During the year ended December 31, 2022, we incurred less than $0.1 million of expenses, consisting of license maintenance fees and reimbursable patent costs, under the WIBR Co-Exclusive Agreement. With respect to the sale of licensed products by us, our affiliates or our sublicensees, WIBR is entitled to receive sub single digit percentage royalties on net sales of licensed products and low single digit percentage royalties on licensed services income until, on a country-by-country basis, the expiration or abandonment of the patent rights. We are entitled to certain customary reductions and offsets on these royalties with respect to a licensed product in a given country. If we sublicense our rights to develop or commercialize a licensed product under the WIBR Co-Exclusive Agreement, WIBR is entitled to a mid-five figure yearly payment for each such sublicense agreement that grants a sublicensee the right under the licensed patents.

Unless earlier terminated, the WIBR Co-Exclusive Agreement will remain in effect until the expiration or abandonment of all licensed patent rights. We may terminate the WIBR Co-Exclusive Agreement at our convenience following written notice to WIBR. Either party may terminate the WIBR Co-Exclusive Agreement for an uncured material breach of the other party. WIBR may also terminate the WIBR Co-Exclusive Agreement in the event that we cease to carry on our business. The last to expire patent under the WIBR Co-Exclusive Agreement, if issued, is expected to expire in 2037.

***Agreements with Acuitas***

*Development and Option Agreement*

In October 2020, we and Acuitas entered into a development and option agreement, or the Acuitas Option Agreement. Under the Acuitas Option Agreement, the parties agreed to jointly develop certain products combining our gene modulating therapeutics with Acuitas's LNPs. Each party granted the other party a worldwide, non-exclusive, royalty-free license under its proprietary technology to conduct the joint research. We will pay Acuitas's personnel costs and external expenses incurred in performing research in accordance with a work plan under the Acuitas Option Agreement. Under the Acuitas Option Agreement, Acuitas granted us options to obtain non-exclusive, worldwide, sublicensable licenses under Acuitas's patent rights and know-how related to LNP technology, or Acuitas LNP Technology, with respect to two specified targets (e.g., OEC constructs), or Reserved Targets, to develop and commercialize one or more therapeutic products including mRNAs that encode the Reserved Targets. For each option and Reserved Target, we are obligated to pay an annual technology access fee and target reservation and maintenance fees collectively in the low-mid six figures until such Reserved

Targets is removed from the Reserved Target list or until we exercise an option with respect to such Reserved Target. On exercise of the first option, we are required to pay a $1.5 million option exercise fee after execution of the first non-exclusive license. On exercise of the second option, we are required to pay a $1.75 million option exercise fee after execution of the second non-exclusive license. During the year ended December 31, 2022, we incurred total expenses of $1.9 million under the Acuitas Option Agreement, consisting of technology access fees, target reservation and maintenance fees, the costs of services performed by Acuitas, the material costs and the reimbursable costs.

Unless earlier terminated, the Acuitas Option Agreement will remain in effect until the first to occur of (1) both options being exercised, and (2) three years from the effective date, except that we can choose to extend the three year term for an additional two years. Either party may terminate the Acuitas Option Agreement for an uncured material breach of the other party or upon the other party's bankruptcy or a similar event. We may terminate the Acuitas Option Agreement at our convenience following written notice to Acuitas. The last to expire patent under the Acuitas Option Agreement, if issued, is expected to expire in 2041.

*License Agreement*

In March 2021, we exercised the first option under the Acuitas Option Agreement and entered into a non-exclusive license agreement with Acuitas, or the Acuitas License Agreement. In connection with the execution of the Acuitas License Agreement, we incurred an expense of $1.5 million for the option exercise fee. Acuitas granted us a non-exclusive, worldwide, sublicensable license under the Acuitas LNP Technology to research, develop, manufacture, and commercially exploit products consisting of our OTX-2002 gene modulating therapeutics and Acuitas's LNPs. The last to expire patent under the Acuitas License Agreement, if issued, is expected to expire in 2041. Under the Acuitas License Agreement, we are required to pay Acuitas an annual license maintenance fee in the high six figures until we achieve a particular development milestone. Acuitas is entitled to receive potential clinical, regulatory, and commercial milestone payments of up to $18.0 million in the aggregate. With respect to the sale of each licensed product by us, our affiliates or our sublicensees, Acuitas is entitled to receive low single digit percentage royalties on net sales of the licensed product in a given country until the last to occur, in such country, of (i) the expiration or abandonment of all licensed patent rights covering the licensed product, (ii) expiration of any regulatory exclusivity for the licensed product, or (iii) ten years from the first commercial sale of the licensed product, or Royalty Term. We are entitled to certain royalty reductions and offsets with respect to each licensed product in a given country if no licensed patents cover the licensed product or if we are required to obtain rights to third party patents that relate to LNP technology.

Unless earlier terminated, the Acuitas License Agreement will remain in effect until the expiration of the last-to-expire Royalty Term. Either party may terminate the Acuitas License Agreement for an uncured material breach of the other party upon the other party's bankruptcy or a similar event. We may terminate the Acuitas License Agreement at our convenience following written notice to Acuitas.

***Collaboration and License Agreement with Nitto***

In October 2022, we entered into a Collaboration and License Agreement (the "Nitto Agreement") with Nitto, pursuant to which, among other things, Nitto granted us an exclusive, worldwide, royalty-bearing, fully transferable and fully sublicensable license under all intellectual property (the "Nitto Licensed IP") owned or controlled by Nitto relating to its LNP delivery technology.

Under the terms of the Nitto Agreement, we paid Nitto an upfront cash payment of $1.0 million. We are also required to make up to $84.0 million in future payments to Nitto based upon the achievement of specified development, regulatory and sales milestones. We are also obligated to pay to Nitto tiered, single-digit percentage royalties on a country-by-country basis based on net sales of the Licensed Product, subject to reduction in specified circumstances.

Unless earlier terminated, the Nitto Agreement will expire on a country-by-country basis when there are no further royalty payments owed by us to Nitto in such country with respect to the licensed product. Upon expiration of the applicable royalty term with respect to the licensed product in a country, the license will become fully paid-up, royalty-free, perpetual and irrevocable with respect to the licensed product in such country. The Nitto Agreement may be terminated by either party upon the other party's uncured material breach of the Nitto Agreement, by either party in the event of the other party's bankruptcy, insolvency or certain similar occurrences,

by us at any time after June 13, 2023 for any or no reason, and by us on a country-by country basis or in its entirety until June 13, 2023 for certain specified good faith reasons.

## Government Regulation

We are subject to extensive regulation. We expect our product candidates to be regulated as biologics. Biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products.

### *U.S. biological products development process*

The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical animal trials and applicable requirements for the humane use of laboratory animals and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLPs;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practice, or GCP, regulations and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current Good Manufacturing Practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

In addition to the IND submission process, sponsors of certain human clinical trials of cells containing recombinant or synthetic nucleic acid molecules, including human gene transfer studies, are subject to evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and

oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution, pursuant to the National Institutes of Health's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

***U.S. review and approval process***

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than the applicant interprets the same data. If the FDA decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of standard BLAs in 10 months from the filing date and 90% of priority BLAs in six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

***Orphan drug designation***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug or biologic was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United

States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

***Expedited development and review programs***

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, product candidates are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the review team during product development and, once an NDA or BLA is submitted, the product may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA or BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA or BLA, the FDA agrees to accept sections of the NDA or BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition. For new-molecular-entity NDAs and original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review).

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In 2017, the FDA established a new regenerative medicine advanced therapy, or RMAT, designation as part of its implementation of the 21st Century Cures Act. The RMAT designation program is intended to fulfill the 21st Century Cures Act requirement that the FDA facilitate an efficient development program for, and expedite review of, any drug or biologic that meets the following criteria: (i) the drug or biologic qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) the drug or biologic is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical

evidence indicates that the drug or biologic has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides all the benefits of breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of clinical trial sites, including through expansion of trials to additional sites.

Fast Track designation, breakthrough therapy designation, priority review, accelerated approval, and RMAT designation do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

***Post-approval requirements***

Biologics are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements up. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in,

among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

***Biosimilars and exclusivity***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are highly similar, or "biosimilar," to or interchangeable with an FDA-approved reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, is generally shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

***Government regulation outside of the United States***

Our product candidates will be subject to similar laws and regulations imposed by jurisdictions outside of the United States, and, in particular, the European Union, or EU, which may include, for instance, clinical trials, marketing authorization, post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. In addition, ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use.

Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product candidates in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

**Non-clinical studies and clinical trials**

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products, or ATMPs. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

***Marketing Authorization***

In order to market our future product candidates in the EU, and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of an

investigational chemical or biological product under EU regulatory systems, we must submit a marketing authorization application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Product for Human Use, or CHMP, of the European Medicines Agency, or EMA, and are valid throughout the EU. The centralized procedure is mandatory for certain types of product candidates, such as (i) medicinal product derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicinal product, (iii) ATMPs such as gene therapy, somatic cell therapy or tissue-engineered medicines and (iv) medicinal product containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a MAA is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs.
- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the above described procedures, the EMA or the competent authorities of the EU member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Under the centralized procedure, the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clockstops. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the Priority Medicines, or PRIME, scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates

these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

***Data and marketing exclusivity.***

In the EU, new product candidates authorized for marketing, or reference product candidates, generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The overall 10-year market exclusivity period may be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

***Pediatric development***

In the EU, MAAs for new medicinal product candidates not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial

data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU member states and study results are included in the product information, even when negative, the product is eligible for a six-month supplementary protection certificate extension or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity is granted.

***Orphan Medicinal Products***

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. In the EU, a medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically-debilitating condition; (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

In the EU, an application for designation as an orphan product must be submitted before the MAA. Orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means during this period, the regulatory authorities cannot accept another MAA, or grant a MA or accept an application to extend a MA, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan drug destination, including where the prevalence of the condition has increased above the threshold or it is judged that the product is sufficiently profitable not to justify maintenance of market exclusivity. Granting of an authorization for another similar orphan medicinal product can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) the applicant cannot supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of medicinal products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

***Brexit and the Regulatory Framework in the United Kingdom***

The United Kingdom, or UK, left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period

provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the Exit Regulations.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain a MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA’s decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

There is no pre-MA orphan designation. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

***Other Healthcare Laws***

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business and may constrain the financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, false claims and transparency laws and regulations with respect to drug pricing and payments and other transfers of value made to physicians and other health care providers. Violations of any of such laws or any other governmental regulations that apply may result in significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or

restructuring of operations, integrity oversight and reporting obligations to resolve allegations of noncompliance, exclusion from participation in federal and state healthcare programs and imprisonment.

***Coverage and Reimbursement***

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing coverage and reimbursement for medical products, drugs and services. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

The U.S. government, state legislatures and foreign governments have also continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

***Healthcare Reform***

In the United States, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended, collectively known as the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to health care, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year, which was temporarily suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, proposed and enacted legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could impact the amounts that federal and state governments and other third-party payors will pay for healthcare products and services.

***Data Privacy & Security***

Numerous state, federal and foreign laws govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. As our operations and business grow, we may become subject to or affected by U.S. federal and state laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain non-U.S. laws govern the privacy and security of personal data, including health-related data, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

***Cybersecurity***

In the normal course of business, we may collect and store personal information and other sensitive information, including proprietary and confidential business information, trade secrets, intellectual property, information regarding trial participants in connection with clinical trials, sensitive third-party information and employee information. To protect this information, our existing cybersecurity policies require continuous monitoring and detection programs, network security precautions, encryption of critical data, and in-depth security assessment of vendors. We maintain various protections designed to safeguard against cyberattacks, including firewalls and virus detection software. We have established and regularly test our disaster recovery plan and we protect against business interruption by backing up our major systems. In addition, we periodically scan our environment for any vulnerabilities, plan to perform penetration testing and engage third parties to assess effectiveness of our data security practices. In addition, we maintain insurance that includes cybersecurity coverage.

Our cybersecurity program is led by a team composed of a highly-skilled third-party security consulting firm and company employees. The program incorporates industry-standard frameworks (such as the NIST Cybersecurity Framework), policies and practices designed to protect the privacy and security of our sensitive information. Our IT team reports to the Audit Committee annually on information security and cybersecurity matters, or as needed.

Despite the implementation of our cybersecurity program, our security measures cannot guarantee that a significant cyberattack will not occur. A successful attack on our information technology systems could have significant consequences to the business. While we devote resources to our security measures to protect our systems and information, these measures cannot provide absolute security. See “Risk Factors – General Risk Factors” for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

### Employees

As of December 31, 2022, we had 116 full-time employees and 1 part-time employee.

### Corporate Information

We were incorporated under the laws of the State of Delaware in July 2016 under the name VL42, Inc.

## Item 1A. Risk Factors.

*You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K, in evaluating our company. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, and the trading price of our common stock could decline. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.*

### Risks Related to Our Financial Condition and Capital Requirements

***We have a limited operating history and no history of successfully developing or commercializing any approved product candidates, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.***

We are a clinical-stage biopharmaceutical company. Our operations to date have been limited to financing and staffing our company, developing our technology and identifying and developing our product candidates. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by biopharmaceutical companies in their early stages of operations. We have not yet demonstrated an ability to conduct or complete any clinical trials, obtain marketing approval, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing, obtaining marketing approval for, and commercializing product candidates. In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other obstacles.

As we continue to build our business, we expect our financial condition and operating results to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

***We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future.***

We have incurred significant net losses since our inception, including net losses of $102.7 million and $68.3 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $237.2 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our preclinical development activities and preparing for and initiating clinical trials of our product candidates.

We expect to continue to incur significant additional net losses for the foreseeable future as we seek to advance product candidates through clinical development, continue preclinical development, expand our research and development activities, develop new product candidates, complete preclinical studies and clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. In order to obtain FDA approval to market any product candidate in the United States, we must submit to the FDA a Biologics License Application, or BLA, demonstrating to the FDA's satisfaction that the product candidate is safe and effective for its intended use(s). Foreign regulatory authorities impose similar requirements. This demonstration requires significant research and extensive data from animal tests, which are referred to as nonclinical or preclinical studies, as well as human tests, which are referred to as clinical trials. Furthermore, the costs of advancing

product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial and difficult to accurately predict. Because of the numerous risks and uncertainties associated with the development of drug products, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if or as we:

- continue our research and development efforts and submit INDs, or similar foreign applications, for our product candidates;
- initiate and conduct clinical trials of our product candidates;
- continue to engineer and develop additional product candidates;
- continue to develop the OMEGA platform;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish manufacturing and supply chain capacity sufficient to provide clinical and, if applicable, commercial quantities of product candidates, including potentially building our own manufacturing facility;
- establish a sales, marketing, internal systems and distribution infrastructure to commercialize any products for which we may obtain regulatory approval, if any, in geographies in which we plan to commercialize our products ourselves;
- maintain, expand, protect and enforce our intellectual property estate;
- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan and support our product development and potential future commercialization efforts;
- enter into collaborations or licenses for new technologies;
- make royalty, milestone, or other payments under our current and any future in-license agreements;
- incur additional legal, accounting, and other expenses in operating our business; and
- continue to operate as a public company.

The amount of future losses and when, if ever, we will achieve profitability are uncertain. We have no commercial-stage products, will not generate revenues from the commercial sale of products until we have successfully developed one or more product candidates, and might never generate revenues from the sale of products. We expect to continue to incur operating losses and negative cash flows for the foreseeable future. These operating losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

***We require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce, or terminate our product development.***

Our operations have incurred substantial expenses since inception. We expect to continue to incur substantial expenses to continue the preclinical development and to initiate and conduct the clinical development of our product candidates, and to continue to identify new product candidates.

We continue to need additional capital beyond the proceeds of our IPO to fund our planned preclinical development and clinical trials, and to develop new product candidates, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Additional sources of financing might not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we might be unable to initiate or complete clinical trials, or seek regulatory approvals, of any of our product candidates from the FDA, or any foreign regulatory authorities, and could be forced to discontinue product development. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our development efforts.

Our existing cash, cash equivalents and marketable securities as of December 31, 2022 will not be sufficient to fund all of our efforts that we plan to undertake. Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of December 31, 2022, together with the net proceeds from the registered direct offering completed on February 27, 2023, will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2024. This estimate is based on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We will require significant additional funds in order to launch and commercialize our current and any future product candidates. In addition, other unanticipated costs may arise in the course of our development efforts. Because most of our product candidates are in preclinical development and we have not conducted any clinical trials, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- the scope, progress, results, and costs of our preclinical studies and clinical trials of OTX-2002 and any future clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for our current and future product candidates in regions where we choose to commercialize any products;
- the number of future product candidates and potential additional indications that we may pursue and their development requirements;
- the stability, scale, yield, and cost of our manufacturing process as we scale-up production and formulation of our product candidates for clinical trials, in preparation for regulatory approval and in preparation for commercialization, including if we pursue plans to build our own manufacturing facility;
- the costs of pre- and post-commercialization activities for any approved product, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- the costs and timing of changes in pharmaceutical pricing and reimbursement infrastructure;
- the costs and timing of changes in the regulatory environment and enforcement rules;
- our ability to compete with other therapeutics in the indications we target;
- the effect of competing technological and market developments;
- the extent to which we enter into collaborations or licenses for products, product candidates, or technologies;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs of preparing, filing, and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims;
- the costs of operating as a public company; and
- the severity, duration, and impact of the COVID-19 pandemic, which may adversely impact our business.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts, on terms acceptable to us, or on a timely basis, we may have to significantly delay, scale back, or discontinue the development or commercialization of our product candidates or other research and development initiatives.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above

events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

***Raising additional capital may cause additional dilution to our stockholders, restrict our operations, require us to relinquish rights to our technologies or product candidates, and could cause our share price to fall.***

Until such time, if ever, as we can generate substantial revenue from product sales, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our operations, our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, redeeming our stock, making certain investments, and engaging in certain merger, consolidation, or asset sale transactions, among other restrictions. If we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***Our existing and any future indebtedness could adversely affect our ability to operate our business.***

As of December 31, 2022, we had $20.0 million of outstanding borrowings under an amended loan and security agreement, the Loan Agreement, with Pacific Western Bank, or PWB. The maturity date of the Loan Agreement is September 30, 2025, and we will be required to begin repayment of the loan in 24 equal monthly payments beginning on September 30, 2023. The outstanding balance under the Loan Agreement bears interest at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%, due monthly starting the first month after December 20, 2021. Pursuant to the terms of the Loan Agreement, interest payment on the outstanding term loan is less than $0.1 million per month, and we are required to pay a success fee of up to $0.2 million upon the occurrence of a specified liquidity event. Our outstanding indebtedness, including any additional indebtedness beyond our borrowings from PWB, combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, product candidate development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our then existing cash and cash equivalents. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under the Loan Agreement or any other debt instruments. Failure to make payments or comply with other covenants under the Loan Agreement or such other debt instruments could result in an event of default and acceleration of amounts due. For example, the affirmative covenants under our Loan Agreement include, among others, covenants requiring us (and us to cause our subsidiaries) to maintain our legal existence and governmental approvals, deliver certain financial reports and notifications, maintain proper books of record

and account, timely file and pay tax returns, maintain inventory and insurance coverage, and maintain cash with PWB (subject to exceptions) and in accounts subject to control agreements (subject to exceptions). Under the Loan Agreement, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and PWB accelerates the amounts due, we may not be able to make accelerated payments and the lender could seek to enforce security interests in the collateral securing such indebtedness. In addition, the covenants under the Loan Agreement, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing.

***We have not generated any product revenue and may never be profitable.***

Our ability to become profitable depends upon our ability to generate product revenue. To date, we have not generated any product revenue and do not expect to generate significant product revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, our product candidates. Most of our product candidates are in the preclinical stages of development and will require additional preclinical studies and clinical development, regulatory review and approval, a secure manufacturing supply, established sales capabilities for commercialization, substantial investment and sufficient funds, and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate product revenue depends on a number of factors, including:

- our ability to complete IND-enabling or other clinical trial-enabling studies and successfully submit INDs or comparable applications to allow us to initiate clinical trials of our product candidates;
- timely initiation and completion of any clinical trials of our product candidates, which may be significantly slower or more costly than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates;
- our ability to demonstrate to the satisfaction of the FDA or similar foreign regulatory authorities the safety and efficacy of our product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates, if any;
- the timely receipt of necessary marketing approvals from the FDA or similar foreign regulatory authorities;
- the willingness of physicians, operators of clinics, and patients to utilize or adopt epigenetic therapeutics;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities, and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMP, or similar regulatory requirements outside the United States;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates, whether alone or in collaboration with others; and
- our ability to establish, maintain, protect, and enforce intellectual property rights in and to our product candidates.

Many of the factors listed above are beyond our control, and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercialize our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates, we may be unable to continue operations without continued funding.

## Risks Related to the Discovery, Development, Preclinical and Clinical Testing, and Regulatory Approval of Our Product Candidates

***Our product candidates are based on a novel technology, which makes it difficult to predict the time and cost of preclinical and clinical development and of subsequently obtaining regulatory approval, if at all.***

Our success depends on the OMEGA platform technology which is a novel technology. As such, it is difficult to accurately predict the preclinical and clinical developmental challenges we may incur for our programs and product candidates as they proceed through product discovery or identification, preclinical studies, and clinical trials. In addition, because we have only recently commenced clinical trials of our pipeline product candidates, we have not yet been able to assess the safety or efficacy of our technology in humans and there may be short-term or long-term effects from treatment with any product candidates that we develop that we cannot predict at this time. Also, animal models may not exist for some of the diseases we choose to pursue in our programs. Given the novelty of our technology platform, there can be no assurance as to the length of preclinical work, clinical development, the number of patients that FDA or comparable foreign regulatory authority may require to be enrolled in clinical trials to establish the safety and efficacy, purity and potency of our product candidates, or that the data generated in these clinical trials will be acceptable to the FDA or comparable foreign regulatory authorities to support marketing approvals. The FDA and comparable regulatory authorities may take longer than usual to come to a decision on any biologics license application, or BLA, or foreign marketing application, that we submit and may ultimately determine that there is not adequate data, information, or experience with our product candidate to support approval. The FDA or comparable foreign regulatory authorities may also require that we conduct additional post-marketing studies or implement risk management programs, such as a risk evaluation and mitigation strategy, or REMS, or similar risk management measures, until more experience with our product candidates are obtained. Each of these factors could increase our expected development costs, and delay, prevent, or limit the scope of any commercialization of our product candidates. The validation process takes time and resources, may require independent third-party analyses, and may not be accepted or approved by the FDA and comparable foreign regulatory authorities. We cannot be certain that our approach will lead to the development of approvable or marketable products, alone, or in combination with other therapies.

Moreover, even if we obtain data from our planned clinical trials, because the OMEGA platform technology applied in our programs is novel and has not been externally verified, our data may be difficult to replicate and/or subject to misinterpretation by us or others. Epigenomic controllers present a new class of medicines and have not been evaluated in clinical trials or received regulatory approval. As a result, we may need to develop new evaluation methods or metrics for clinical data, which may make it more difficult to analyze data, or it may take more time or be more costly for us to develop our OECs than other therapeutics for the same indications. As a result of these factors, it is difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of the OMEGA platform technology, or any similar or competitive epigenetic technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development challenges we experience in the future related to the OMEGA platform technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use as well as market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities and approaches. Further, as we are developing novel treatments, there is heightened risk that the FDA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, few gene therapy products have been approved by the FDA and comparable foreign regulatory authorities, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union, or EU, or other jurisdictions. Further, approvals by one regulatory authority may not be indicative of what other regulatory authorities may require for approval.

Regulatory requirements governing programmable epigenetic medicines have evolved and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within

its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In addition to FDA oversight and oversight by IRBs, under guidelines promulgated by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Before a clinical study can begin at any institution, that institution's IRB, and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. These and other regulatory review agencies, committees, and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. Similar requirements apply in the EU. The European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, which is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products, or ATMP(s). ATMPs include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for ATMP candidate that is submitted to the EMA. In the EU, the development and evaluation of an ATMP must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape.

Changes in applicable regulatory guidelines may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates, or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with regulatory authorities and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

***No epigenomic controller medicines have been approved in this potentially new class of medicines, and may never be approved as a result of efforts by others or us. mRNA drug development has substantial development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.***

As a potential new category of medicines, no epigenomic controller medicines have been approved to date by the FDA or other regulatory authority. Successful discovery and development of epigenomic controller medicines by either us or our strategic collaborators is highly uncertain and depends on numerous factors, many of which are beyond our or their control. We have made and will continue to make a series of business decisions and take calculated risks to advance our development efforts and pipeline, including those related to mRNA technology, delivery technology, and manufacturing processes which may be shown to be incorrect based on further work by us, our strategic collaborators, or others.

Our medicines that appear promising in the early phases of development may fail to advance, experience delays in preclinical stages or the clinic, experience clinical holds, or fail to reach the market for many reasons, including:

- discovery efforts at identifying potential epigenomic controller medicines may not be successful;

- nonclinical or preclinical study results may show potential epigenomic controller medicines to be less effective than desired or to have harmful or problematic side effects;
- clinical trial results may show the epigenomic controller medicines to be less effective than expected (e.g., a clinical trial could fail to meet one or more endpoints) or to have unacceptable side effects or toxicities;
- adverse effects in any one of our preclinical studies or clinical trials or adverse effects relating to our mRNA, or lipid nanoparticles, or LNPs, may lead to delays in or termination of one or more of our programs; and
- the insufficient ability of our translational models to reduce risk or predict outcomes in humans, particularly given that each component of our investigational medicines and development candidates, may have a dependent or independent effect on safety, tolerability, and efficacy, which may, among other things, be species-dependent.

Our investigational medicines are currently formulated and administered in an LNP. These LNPs may cause systemic side effects related to the components of the LNP and some may have not yet been tested in humans. A recognized limitation of LNPs is the potential for inflammatory reactions upon single and repeat administration that can impact tolerability and therapeutic index. Our licensed and internally developed, proprietary LNP systems are therefore designed to be highly tolerated and minimize LNP vehicle-related toxicities with repeat administration in vivo. While we continue to optimize our LNPs, there can be no assurance that our LNPs will not have undesired effects. Certain aspects of our investigational medicines may induce immune reactions from either the mRNA or the lipid as well as adverse reactions within biological pathways or due to degradation of the mRNA or the LNP, any of which could lead to significant adverse events in one or more of our preclinical or clinical studies. Our LNPs could contribute, in whole or in part, to one or more of the following: immune reactions, infusion reactions, complement reactions, opsonation reactions, antibody reactions including IgA, IgM, IgE or IgG or some combination thereof, or reactions to the polyethylene glycol, or PEG, from some lipids or PEG otherwise associated with the LNP. Many of these types of side effects have broadly been observed for LNPs. There may be resulting uncertainty as to the underlying cause of any such adverse event, which would make it difficult to accurately predict side effects in future clinical trials and would result in significant delays in our programs.

***Preclinical development is uncertain, especially for a new class of medicines such as epigenomic controllers, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance into the clinic, any of which may a have a material adverse impact on our platform or our business.***

Most of our programs are in preclinical development. Before we can initiate clinical trials for a development candidate, we must complete extensive preclinical studies, including IND-enabling good laboratory practices, or GLP, and equivalent requirements outside the United States, toxicology testing. Preclinical development is uncertain, including due to variability in the disease models used. We may not identify development candidates with the treatment activity or safety characteristics required to advance them into further preclinical studies or results from preclinical studies of initially promising development candidates may not support further testing. We must also complete extensive work on Chemistry, Manufacturing, and Controls, or CMC, activities (including yield, purity and stability data) to be included in any IND or similar foreign filing. CMC activities for a new class of medicines such as epigenomic controllers require extensive manufacturing processes and analytical development, which is uncertain and lengthy. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept the results of our preclinical testing or our proposed clinical programs or if the outcome of our preclinical testing, studies, and CMC activities will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

***Clinical development of OTX-2002 may be delayed or terminated, and we may never obtain regulatory approval of OTX-2002, which may have a material adverse impact on our platform or our business. Furthermore, clinical development requires substantial capital investment, which we may not be able to support. We may incur unforeseen costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of OTX-2002 and our other product candidates.***

Before obtaining marketing approval from the FDA or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, time-consuming, and subject to uncertainty. A failure of one or more clinical trials can occur at any stage of the process, and the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

In July 2022, we announced clearance of our IND application from the FDA to initiate a Phase 1/2, first-in-human, clinical trial of OTX-2002 for the treatment of HCC, which has launched under the MYCHELANGELO clinical program. We have not initiated or completed any other clinical trials for any of our product candidates. We cannot guarantee that any of our clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We also cannot be sure that submission of any future IND or similar application will result in the FDA or other regulatory authority, as applicable, allowing future clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in reaching a consensus with regulatory authorities on trial design or implementation of the clinical trials;
- delays or failure in obtaining regulatory authorization to commence a trial;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among CROs and clinical trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- delays in obtaining required institutional review board, or IRB, or ethics committee approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing, or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities for a number of reasons, including after review of an IND or amendment or equivalent foreign application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- delays in recruiting, screening, and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, clinical sites, other third parties or us to adhere to clinical trial protocols, to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements, or GCPs, or similar applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;

- clinical sites dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract development and manufacturing organization, or CDMO, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter difficulties or delays in initiating, enrolling, conducting, or completing our planned and ongoing clinical trials. Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue from product sales. Clinical trial delays could also shorten any periods during which any approved products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may seriously harm our business.

Clinical trials must be conducted in accordance with the legal requirements, regulations, or guidelines of the FDA and other applicable regulatory authorities and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board, or DSMB, for such trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, which could significantly reduce the commercial viability of our

product candidates. Any of these occurrences may harm our business, financial condition, results of operations, and prospects significantly.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical trial development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

It is currently unclear to what extent the United Kingdom, or UK, will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency, or MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the UK chooses to align with the regulation or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

***The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, expensive, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be seriously harmed.***

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate in the United States or any other jurisdiction, and it is possible that any product candidates we may seek to develop in the future will never obtain regulatory approval.

Prior to obtaining approval to commercialize a product candidate in the United States or elsewhere, we must demonstrate with substantial evidence from well-controlled trials, and to the satisfaction of the FDA, or other regulatory authorities, that such product candidates are safe and effective, pure, and potent for their intended uses. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA or other regulatory authorities. The FDA or other regulatory authorities may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program.

The FDA or any foreign regulatory authorities can delay, limit, or deny approval of our product candidates, or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including, but not limited to, the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation, or interpretation of results of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective, pure, and potent for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required for approval by the FDA or comparable foreign regulatory authorities;
- serious and unexpected product candidate-related side effects experienced by participants in our clinical trials or by individuals using products similar to our product candidates;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a BLA or other submission, or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may disagree regarding the formulation, labeling, and/or the specifications of our product candidates;
- our clinical sites, investigators or other participants in our clinical trials may deviate from a trial protocol, fail to conduct the trial in accordance with regulatory requirements, or drop out of a trial;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would seriously harm our business.

Even if we eventually complete clinical trials and obtain approval of a BLA or foreign marketing application for our product candidates, the FDA, or comparable foreign regulatory authorities may grant approval contingent on the performance of costly additional trials, including Phase 4 clinical trials, and/or the implementation of a REMS or similar risk management measures, which may be required to ensure the benefits of the drug outweigh its risks after approval. The FDA or comparable foreign regulatory authorities may also approve a product candidate for a more limited indication or patient population than we originally requested. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate, and would materially adversely impact our business and prospects.

***Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.***

Adverse events or other undesirable side effects caused by our product candidates could cause us, any DSMB for a trial, or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled

patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, results of operations, and prospects significantly.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer, and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts, and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.

If any serious adverse events occur during clinical development, clinical trials of any product candidates or products we develop could be suspended or terminated, and our business could be seriously harmed. Treatment-related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us to cease further development of, or deny approval of any product candidates for any or all targeted indications. If we are required to delay, suspend, or terminate any clinical trial, the commercial prospects of such product candidates may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if one or more of our product candidates receives marketing approval and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may suspend, limit, or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a REMS or similar risk management measures which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions, or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

***Our company has never commercialized a product candidate and may experience delays or unexpected difficulties in obtaining regulatory approval for our current and future product candidates.***

We have never obtained regulatory approval for, or commercialized any product candidate. It is possible that the FDA may refuse to accept any or all of our planned BLAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any product candidates. If the FDA does not approve any of our planned BLAs, it may require that we conduct additional costly clinical trials, preclinical studies or CMC studies before it will reconsider our applications. Depending on the extent of these or any other FDA required studies, approval of any BLA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any BLA or other application that we submit. Similar risks may exist in foreign jurisdictions. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

***If we encounter difficulties enrolling patients in any clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the target disease population;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- competing clinical trials for similar therapies or other new therapeutics not involving our product candidates and or related technologies;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before trial completion; and
- other factors outside of our control, such as the COVID-19 pandemic.

In addition, our planned clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates or similar areas, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, which could prevent completion or commencement of these trials and adversely affect our ability to advance the development of our product candidates.

***Interim, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data

and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

***We may not be successful in our efforts to identify and successfully develop additional product candidates.***

Part of our strategy involves identifying novel product candidates. The OMEGA platform may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third-parties' patent or other intellectual property or exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities, or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance, if approved;
- potential product candidates may not be effective in treating their targeted diseases or symptoms;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is highly complex and difficult to navigate successfully or economically.

If we are unable to identify and successfully commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

***We have received orphan drug designation from the FDA for OTX-2002 for the treatment of HCC, and we may seek orphan drug designation for additional product candidates in the future, but we may be unable to obtain such designations or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced.***

Regulatory authorities in some jurisdictions, including the United States, may designate drugs or biologics intended to treat relatively small patient populations as orphan drug products. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

In the United States, orphan drug designation entitles a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available

for clinical trials of drugs or biologics for rare diseases, regardless of whether the drugs or biologics are designated for the orphan use. In addition, if a drug or biologic with an orphan drug designation subsequently receives the first marketing approval for the disease or condition for which it has such designation, the product is entitled to a seven year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same disease or condition for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the "same drug" and treat the same diseases or conditions as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

We have obtained orphan drug designation from the FDA for OTX-2002 for the treatment of HCC. We may seek orphan designation for certain of our future product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these and may be unable to maintain the benefits associated with orphan drug designation. Even if we obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA from approving the same or a different drug for another disease or condition. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan-drug-exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

***We have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. Such investments may affect our operating results, and, if the return on these investments is lower or develops more slowly than we expect, our revenue and operating results may suffer.***

We use our technological capabilities for the discovery of new product candidates and, since our inception, we have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. These investments may involve significant time, risks, and uncertainties, including the risk that the expenses associated with these investments may affect our margins and operating results and that such investments may not generate sufficient technological advantages relative to alternatives in the market, which would in turn, impact revenues to offset liabilities assumed and expenses associated with these new investments. The biotechnology industry changes rapidly as a result of technological and product developments, which may render our platform's ability to identify and develop product candidates less efficient than other technologies and platforms. We believe that we must continue to invest a significant amount of time and resources in the OMEGA platform to maintain and improve our competitive position. If we do not achieve the benefits anticipated from these investments, if the achievement of these benefits is delayed, or if our technology is not able to accelerate the process of drug discovery as quickly as we anticipate, our revenue and operating results may be adversely affected.

***We must adapt to rapid and significant technological change and respond to introductions of new products and technologies by competitors to remain competitive.***

In addition to using our platform for the discovery and development of our own product candidates, we collaborate with other biopharmaceutical and pharmaceutical companies in the discovery and development of our OEC. The technological landscape around artificial intelligence and precision drug design is characterized by significant enhancements and evolving industry standards. As a result, our and our collaborators' needs are rapidly evolving. If we do not appropriately innovate and invest in new technologies, our platform may become less competitive, and our collaborators could move to new technologies offered by our competitors, or engage in drug discovery themselves. We believe that because of the initial time investment required by many of our collaborators to reach a decision about whether to collaborate with us, it may be difficult to regain a commercial relationship with such collaborator should they enter into a partnership or collaboration agreement with a competitor. Without the timely introduction of new solutions and technological enhancements, our offerings will

likely become less competitive over time, in which case our competitive position and operating results could suffer. Accordingly, we focus significant efforts and resources on the development and identification of new technologies and markets to further broaden and deepen our capabilities and expertise in drug discovery and development. For example, to the extent we fail to timely introduce new and innovative technologies or solutions, adequately predict our collaborators' needs or fail to obtain desired levels of market acceptance, our business may suffer and our operating results could be adversely affected.

***The potential market opportunities for our product candidates may be smaller than we anticipated or may be limited to those patients who are ineligible for or have failed prior treatments, and our estimates of the prevalence of our target patient populations may be inaccurate.***

Our current and future target patient populations are based on our beliefs and estimates regarding the incidence or prevalence of certain types of cancers that may be addressable by our product candidates, which is derived from a variety of sources, including scientific literature and surveys of clinics. Our projections may prove to be incorrect and the number of potential patients may turn out to be lower than expected. Even if we obtain significant market share for our product candidates, because the potential target populations could be small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use of our product candidates for front-line and second-line therapy.

Cancer therapies are sometimes characterized by line of therapy (first-line, second-line, third-line, etc.), and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first-line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second-line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third-line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of some of our product candidates as second- or third-line therapies for patients who have failed other approved treatments. Subsequently, for those product candidates that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second-line therapy and potentially as a first-line therapy, but there is no guarantee that our drug candidates, even if approved for third-line therapy, would be approved for second-line or first-line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second-line or first-line therapy.

***We may focus on potential product candidates that may prove to be unsuccessful and we may have to forego opportunities to develop other product candidates that may prove to be more successful.***

We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful, or to license or purchase a marketed product that does not meet our financial expectations. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify and successfully commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

Furthermore, we have limited financial and personnel resources and are placing significant focus on the development of our lead product candidates, and as such, we may forgo or delay pursuit of opportunities with other future product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate, we may relinquish valuable rights to those future product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future product candidates.

***We may pursue Fast Track, breakthrough, and regenerative medicine advanced therapy designation by FDA. These designations may not actually lead to a faster development or regulatory review or approval process, and they do not assure FDA approval of any product candidates we may develop.***

FDA's Fast Track, breakthrough, and regenerative medicine advanced therapy, or RMAT, programs are intended to expedite the development of certain qualifying products intended for the treatment of serious diseases and conditions. If a product candidate is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the product's potential to address an unmet medical need for this condition, the sponsor may be eligible for FDA Fast Track designation. A product candidate may be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A product candidate may receive RMAT designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening condition, and preliminary clinical evidence indicates that the product candidate has the potential to address an unmet medical need for such condition. While we may seek Fast Track, breakthrough, and/or RMAT designation, there is no guarantee that we will be successful in obtaining any such designation. Even if we do obtain such designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. A Fast Track, breakthrough, or RMAT designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. In addition, the FDA may withdraw Fast Track, breakthrough, or RMAT designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track, breakthrough, and/or RMAT designation alone do not guarantee qualification for the FDA's priority review procedures.

***Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.***

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties, and costs for us and may require additional preclinical studies or clinical trials which would be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain, and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

***Even if a current or future product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.***

If any current or future product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement, including with respect to the use of the approved product as a combination therapy;
- adoption of a companion diagnostic and/or complementary diagnostic; and
- the prevalence and severity of any side effects.

***Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain, or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.***

The ability of the FDA and foreign regulatory authorities to review or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA, following its relocation to Amsterdam and related reorganization (including staff changes), may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the U.S. have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities, which could have a material adverse effect on our business. If a prolonged government shutdown occurs, or if global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

***Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.***

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, property, auto, employment practices, workers' compensation, environmental liability, and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates we develop. Although our environment liability insurance provides certain coverage for claims attributable to the release of biological or hazardous materials, our property, casualty, and general liability insurance policies

specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Operating as a public company has and will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash and cash equivalents position and results of operations.

## Risks Related to Healthcare Laws and Other Legal Compliance Matters

***We will be subject to extensive and costly government regulation.***

Our product candidates will be subject to extensive and rigorous domestic government regulation, including regulation by the FDA, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments, and their respective equivalents outside of the United States. The FDA regulates the research, development, preclinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, and export of pharmaceutical products. If our products are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not they have obtained FDA approval for a given product and its uses. Such foreign regulation may be equally or more demanding than corresponding United States regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. We must obtain and maintain regulatory authorization to conduct preclinical studies and clinical trials. We must obtain regulatory approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires the submission of extensive preclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy, potency, and purity, for each intended use. The development and approval process takes many years, requires substantial resources, and may never lead to the approval of a product.

Even if we are able to obtain regulatory approval for a particular product, the approval may limit the indicated medical uses for the product, may otherwise limit our ability to promote, sell, and distribute the product, may require that we conduct costly post-marketing surveillance, and/or may require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, may require further regulatory review and approval. Once obtained, any approvals may be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our consultants, CDMOs, CROs, or other vendors, fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal of a regulatory authority, including the FDA or other regulatory authorities, to review pending market approval applications or supplements to approved applications; warning letters; fines; import and/or export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications or licenses; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

***Enacted and future healthcare legislation and policies may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and could adversely affect our business.***

In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could prevent or delay marketing approval of our products in development, restrict or regulate post-approval activities involving any product candidates for which we obtain marketing approval, impact pricing and reimbursement and impact our ability to sell any such products profitably. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. In addition, new regulations and interpretations of existing healthcare statutes and regulations are frequently adopted.

In March 2010, the Patient Protection and Affordable Care Act, or ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect as of the date of this report through 2031, unless additional Congressional action is taken. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the orphan drug tax credit was reduced

as part of a broader tax reform. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other healthcare funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as outcomes-based reimbursement. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic, and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. EU member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. EU member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval in some EU member states, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local standard of care. Other EU member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. Generally, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict, or regulate post-approval activities, and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In addition, in the United States, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be

sure whether additional legislative changes will be enacted, or whether the FDA's regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***If our product candidates obtain regulatory approval, we and they will be subject to ongoing regulatory review and significant post-market regulatory requirements and oversight.***

If the FDA or other regulatory authorities approve any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and record-keeping of our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submission of safety and other post-marketing information and reports, registration, as well as ongoing compliance with cGMPs and similar foreign requirements and GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers of biological products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities to ensure compliance with cGMP regulations and similar foreign requirements. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, any regulatory approvals that we may receive for our product candidates may contain significant limitations related to use restrictions for specified age groups, warnings, precautions, or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training, and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

Failure to comply with applicable regulatory requirements, may subject us to administrative or judicially imposed sanctions, including:

- delays in reviewing or the rejection of product applications or supplements to approved applications;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- warning or untitled letters;
- civil or criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions, or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on our operations, including costly new manufacturing requirements.

The occurrence of any such event may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

Moreover, the policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product

candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***The Hatch-Waxman Act in the United States provides for the opportunity to seek a patent term extension on one selected patent for each of our products, and the length of that patent term extension, if at all, is subject to review and approval by the U.S. Patent and Trademark Office, or the USPTO, and the FDA.***

In the United States, the Hatch-Waxman Act permits one patent term extension of up to five years beyond the normal expiration of one patent per product, which if a method of treatment patent, is limited to the approved indication (or any additional indications approved during the period of extension). The length of the patent term extension is typically calculated as one half of the clinical trial period plus the entire period of time during the review of the BLA by the FDA, minus any time of delay by us during these periods. There is also a limit on the patent term extension to a term that is no greater than fourteen years from drug approval. Therefore, if we select and are granted a patent term extension on a recently filed and issued patent, we may not receive the full benefit of a possible patent term extension, if at all. We might also not be granted a patent term extension at all, because of, for example, failure to apply within the applicable period, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authorities in other countries, may not agree with our assessment of whether such extensions are available, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate product revenue.

In 1997, as part of the Food & Drug Administration Modernization Act, or FDAMA, Congress enacted a law that provides incentives to drug manufacturers who conduct studies of drugs in children. The law, which provides six months of exclusivity in return for conducting pediatric studies, is referred to as the pediatric exclusivity provision. If clinical studies are carried out by us that comply with the FDAMA, we may receive an additional six-month term added to any regulatory data exclusivity period and our patent term extension period, if received, on our product. However, if we choose not to carry out pediatric studies that comply with the FDAMA, or are not accepted by the FDA for this purpose, we would not receive this additional six-month exclusivity extension to our data exclusivity or our patent term extension.

In the EU, supplementary protection certificates, or SPCs, are available to extend a patent term up to five years to compensate for patent term lost during regulatory review, and can be extended (if any is in effect at the time of approval) for an additional six months if data from clinical trials is obtained in accordance with an agreed-upon pediatric investigation plan. Although all EU member states must provide SPCs, SPCs must be applied for and granted on a country-by-country basis. This can lead to a substantial cost to apply for and receive these certificates, which may vary among countries or not be granted at all***.***

***Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.***

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which makes it illegal for any person to knowingly and willfully solicit, offer, receive, pay, or provide any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to

have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false, fictitious, or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease, or conceal an obligation to pay money to the U.S. federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the Federal Food, Drug and Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics, and medical devices;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance

guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock or stock options for services provided to us and may be in the position to influence the ordering of or use of our product candidates, if approved, may not comply with current or future statutes, regulations, agency guidance, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight, and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

***We are subject to governmental regulation and other legal obligations, particularly related to privacy, data protection and information security. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.***

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. We do not believe that we are currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations, which govern the privacy, processing and protection of health-related and other personal information. For example, on June 28, 2018, California enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers, increases the privacy and security obligations of entities handling certain personal information, requires certain disclosures to California individuals, affords such individuals new abilities to opt out of certain sales of personal information, and provides for civil penalties for violations as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act, or CPRA, recently passed in California. The CPRA significantly amends the CCPA and will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance

investment and potential business process changes may be required. Complying with these numerous, complex, and often changing regulations is expensive and difficult, and failure to comply with any privacy laws or data security laws or any security incident or breach involving the misappropriation, loss or other unauthorized processing, use or disclosure of sensitive or confidential patient, consumer or other personal information, whether by us, one of our CROs or another third party, could adversely affect our business, financial condition, and results of operations, including but not limited to: investigation costs; material fines and penalties; compensatory, special, punitive, and statutory damages; litigation; consent orders regarding our privacy and security practices; requirements that we provide notices, credit monitoring services, and/or credit restoration services or other relevant services to impacted individuals; adverse actions against our licenses to do business; reputational damage; and injunctive relief. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Our activities outside the United States may be subject to additional compliance requirements and generate additional risks of enforcement for noncompliance. For example, on May 25, 2018, the General Data Protection Regulation, or GDPR, went into effect and imposes strict requirements for processing the personal data of individuals within the EEA. For example, the GDPR applies extraterritorially, and requires us to make detailed disclosures to data subjects, disclose the legal basis on which we can process personal data, to obtain valid consent for collecting and processing personal data (including data from clinical trials), appoint data protection officers when sensitive personal data, such as health data, is processed on a large scale, provides robust rights for data subjects, and adopt appropriate privacy governance, including policies, procedures, training, and data audit. It also imposes mandatory data breach notification and certain obligations on us when contracting with service providers. The GDPR provides that EEA countries may establish their own laws and regulations limiting the processing of personal data, including genetic, biometric, or health data, which could limit our ability to use and share personal data or could cause our costs to increase. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States. For example, in 2016, the EU and United States agreed to a transfer framework for data transferred from the EU to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union, or CJEU. In March 2022, the United States and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-U.S. Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. Further, while the CJEU upheld the adequacy of the standard contractual clauses, or SCCs, it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the SCCs must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on to state that if a competent supervisory authority believes that the SCCs cannot be complied with in the destination country and the required level of protection cannot be secured by other means, such supervisory authority is under an obligation to suspend or prohibit that transfer. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. The revised SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom; the United Kingdom's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021.

Additionally, from January 2021, we have to comply with the GDPR and the United Kingdom GDPR, each regime having the ability to fine up to the greater of €20 million (£17.5 million) or 4% of global turnover for violations. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term. The European Commission has adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless the

European Commission re-assesses and renews/extends that decision, and remains under review by the Commission during this period. In September 2021, the United Kingdom government launched a consultation on its proposals for wide-ranging reform of United Kingdom data protection laws following Brexit. These changes may lead to additional costs and increase our overall risk exposure. In addition, we may be the subject of litigation and/or adverse publicity, which could adversely affect our business, results of operations, and financial condition.

We cannot assure you that our CDMOs, CROs or other third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations, and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, use, storage, and transmission of such information. Moreover, patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business. If we or third-party CDMOs, CROs, or other contractors or consultants fail to comply with applicable federal, state, or local regulatory privacy requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing, and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security, or reputational damage. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities***.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws, and regulations. These laws and regulations govern, among other things, the controlled use, handling, release, and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds, and compounds that have a toxic effect on reproduction, laboratory procedures, and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

***We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally.***

Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with applicable laws and regulations, our policies, and other legal or contractual requirements, which may give rise to regulatory enforcement action, liability, lead to the loss of trade secrets or other intellectual property or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. Furthermore,

negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image, and goodwill. Any of these events could have a material adverse effect on our business, prospects, financial condition, and results of operations, and could adversely affect the price of our common stock.

## Risks Related to Commercialization

***We are very early in our development efforts. Most of our product candidates are in preclinical development or discovery and we recently received FDA clearance for our IND application for OTX-2002 and have initiated the associated clinical trial. It will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.***

We are very early in our development efforts and have focused our research and development efforts to date on developing the OMEGA platform, identifying our initial targeted disease indications and engineering our initial OECs. We have only conducted in vivo preclinical studies for some of our programs and there is no guarantee that we will conduct preclinical in vivo studies for other programs. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of our product candidates, which may never occur.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND or by foreign regulatory authorities of a similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA or foreign regulatory authorities require us to complete additional preclinical studies or we are required to satisfy other FDA or foreign regulatory authorities requests, the start of our clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or change their position on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

Commercialization of our product candidates will require additional preclinical and clinical development and regulatory and marketing approval. Our ability to conduct development or attain marketing approval will depend on the sufficiency of our financial and other resources to complete the necessary preclinical studies, IND-enabling studies or similar studies, and clinical trials and the successful enrollment in, and completion of, clinical trials.

If we do not successfully achieve one or more of these activities in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

***Developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets.***

Our industry has been characterized by extensive research and development efforts, rapid developments in technologies, intense competition, and a strong emphasis on proprietary products. We expect our product candidates to face intense and increasing competition as new products enter the relevant markets and advanced technologies become available. We face potential competition from many different sources, including pharmaceutical, biotechnology, and specialty pharmaceutical companies. Academic research institutions, governmental agencies, and public and private institutions are also potential sources of competitive products and technologies. Our competitors may have or may develop superior technologies or approaches, which may provide them with competitive advantages. Many of these competitors may also have compounds already approved or in development in the therapeutic categories that we are targeting with our product candidates. In addition, many of these competitors, either alone or together with their collaborators, may operate larger research and development programs or have substantially greater financial resources than we do, as well as greater experience in:

- developing product candidates;
- undertaking preclinical testing and clinical trials;

- obtaining BLA approval by the FDA or comparable foreign regulatory approvals of product candidates;
- formulating and manufacturing products; and
- launching, marketing, and selling products.

If these competitors access the marketplace before we do with safer, more effective, or less expensive therapeutics, our product candidates, if approved for commercialization, may not be profitable to sell or worthwhile to continue to develop. Technology in the pharmaceutical industry has undergone rapid and significant change, and we expect that it will continue to do so. Any compounds, products, or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development. The success of our product candidates will depend upon factors such as product efficacy, safety, reliability, availability, timing, scope of regulatory approval, acceptance and price, among other things. Other important factors to our success include speed in developing product candidates, completing clinical development and laboratory testing, obtaining regulatory approvals and manufacturing, and selling commercial quantities of potential products.

We may face competition from new entrants to the epigenetic medicine space. We also compete with many companies that are using other technologies targeting the same indications we are currently pursuing. We expect our product candidates to compete with companies developing technologies that focus on gene-expression control using various technologies, such as CRISPR gene editing, gene therapies, non-coding RNA therapeutics, and small-molecule epigenetics, including Alnylam Pharmaceuticals Inc., Beam Therapeutics, Inc., Biogen Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Ionis Pharmaceuticals, Inc., Janssen Pharmaceuticals, Inc., Pfizer Inc., and Sangamo Therapeutics, Inc. Even if approved and commercialized, our product candidates may fail to achieve market acceptance with hospitals, physicians, or patients. Hospitals, physicians, or patients may conclude that our products are less safe or effective or otherwise less attractive than existing drugs. If our product candidates do not receive market acceptance for any reason, our revenue potential would be diminished, which would materially adversely affect our ability to become profitable.

Many of our competitors have substantially greater capital resources, robust product candidate pipelines, established presence in the market, and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. As a result, our competitors may achieve product commercialization or patent or other intellectual property protection earlier than we can. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified clinical, regulatory, scientific, sales, marketing, and management personnel, and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or noncompetitive.

***Our product candidates may face competition sooner than anticipated.***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of its product.

We believe that any of our future product candidates approved as a biological product under a BLA should qualify for the twelve-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. Jurisdictions in addition to the United States have established abbreviated pathways for

regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

***The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.***

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs and biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates.

In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare program is increasingly used as a model for how private and other governmental payors develop their coverage and reimbursement policies for new drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in the EU and other jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the

United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

***If we are unable to establish sales, marketing, and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing any of our product candidates, if approved, and we may not be able to generate any product revenue.***

We have limited personnel or infrastructure for the sales, marketing, or distribution of products, and no experience as a company in commercializing a product candidate. The cost of building and maintaining such an organization may exceed the cost-effectiveness of doing so.

We may build our own focused sales, distribution and marketing infrastructure to market our product candidates, if approved, in the United States and other markets around the world. There are significant expenses and risks involved with building our own sales, marketing, and distribution capabilities, including our ability to hire, retain, and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidate, if approved. Additionally, if the commercial launch of our product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our future products;
- our inability to equip medical and sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding applicable diseases and our future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- our inability to develop or obtain sufficient operational functions to support our commercial activities; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable or decide not to establish internal sales, marketing, and distribution capabilities, or decide not to do so for a particular country, we may pursue collaborative arrangements. If we pursue a collaborative arrangement, our sales will largely depend on the collaborator’s strategic interest in the product and such collaborator’s ability to successfully market and sell the product.

If we are unable to build our own sales force or access a collaborative relationship for the commercialization of any of our product candidates, we may be forced to delay the potential commercialization of our product candidates or reduce the scope of our sales or marketing activities for such product candidates. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborators at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to any

of our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results, and prospects.

If we are unable to establish adequate sales, marketing, and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our other product candidates and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In addition, even if we do establish adequate sales, marketing, and distribution capabilities, the progress of general industry trends with respect to pricing models, supply chains, and delivery mechanisms, among other things, could deviate from our expectations. If these or other industry trends change in a manner which we do not anticipate or for which we are not prepared, we may not be successful in commercializing our product candidates or become profitable.

***Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future profitability may depend, in part, on our ability to commercialize our product candidates, if approved, in foreign markets, including the EU, for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approvals in other countries, we may be required to comply with numerous and varying regulatory requirements of such countries regarding the safety and efficacy of our product candidates and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities if we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting, and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- our ability to supply our product candidates on a timely and large-scale basis in local markets;
- longer lead times for shipping which may necessitate local manufacture of our product candidates;
- language barriers for technical training and the need for language translations;
- reduced protection of patent and other intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions, and changes in tariffs.

If any of our product candidates is approved for commercialization, we may selectively partner with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries, including requirements specific to biologics or gene therapy products;
- reduced protection for patent and other intellectual property rights;
- foreign reimbursement, pricing, and insurance regimes;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions;
- political unrest and wars, such as the conflict between Russia and Ukraine, which could delay or disrupt business activity, and if such political unrest escalates or spills over to or otherwise impacts additional regions, it could heighten many of the other risk factors described in this Item 1A; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor, and other legal requirements imposed by both the EU and many of the individual EU member states with which we will need to comply. Many U.S.-based biotechnology companies have found the process of marketing their own products in the EU to be very challenging.

Certain legal and political risks are also inherent in foreign operations. There is a risk that foreign governments may nationalize private enterprises in certain countries where we may operate. In certain countries or regions, terrorist activities, political unrest and wars, such as the conflict between Russia and Ukraine, and the response to such activities may threaten our operations more than in the United States. Social and cultural norms in certain countries may not support compliance with our corporate policies, including those that require compliance with substantive laws and regulations. Also, changes in general economic and political conditions in countries where we may operate are a risk to our financial performance and future growth. Additionally, the need to identify financially and commercially strong partners for commercialization outside the United States who will comply with the high manufacturing and legal and regulatory compliance standards we require is a risk to our financial performance. As we operate our business globally, our success will depend, in part, on our ability to anticipate and effectively manage these and other related risks. There can be no assurance that the consequences of these and other factors relating to our international operations will not have an adverse effect on our business, financial condition, or results of operations.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials that compare the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

***Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.***

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs, which may not be covered by insurance. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- injury to our reputation;
- initiation of investigations by regulators;
- significant costs to defend the related litigation and related litigation;

- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize a product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources, and the inability to commercialize any product candidate;
- decreased demand for a product candidate, if approved for commercial sale; and
- loss of revenue.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we plan to obtain clinical trial insurance, our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

## Risks Related to our Dependence on Third Parties and Manufacturing

***Our ability to manufacture our OEC candidates for preclinical or clinical supply could be limited, especially with the increased demand for the manufacture of mRNA- and LNP-based vaccines to treat COVID-19, which could adversely affect our development plans.***

We rely on third-party CDMOs of mRNA therapeutics and lipid excipients, a lipid that serves as the vehicle or medium for a drug or other active substance, to manufacture our preclinical and clinical supply of our OEC candidates. Vaccines to treat COVID-19 include mRNA vaccines and vaccines that utilize lipid excipients. Several vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA, and more may be authorized in the coming months. As a result, there is unprecedented demand on these CDMOs to manufacture COVID-19 vaccines and capacity for non-COVID-19 vaccines is limited and may be further limited by the potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, which may make it more difficult to obtain materials or manufacturing slots for the products needed for our planned clinical trials. While we are working to obtain sufficient supply of our OECs for our anticipated preclinical and clinical development, we may experience supply constraints and disruptions as manufacturers prioritize supply for COVID-19 vaccines over our OECs. If we are unable to obtain the supplies we need at a reasonable price or on a timely basis or in the amounts we desire, our ability to complete the development of our OEC candidates or, if we obtain regulatory approval for our OEC candidates, to commercialize them, could be materially adversely affected.

***Our OEC candidates are based on novel technology and may be complex and difficult to manufacture. We may encounter difficulties in manufacturing, product release, shelf life, testing, storage, supply chain management, or shipping.***

Due to the novel nature of our technology and limited experience at larger scale production, we may encounter difficulties in manufacturing, product release, shelf life, testing, storage and supply chain management, or shipping. These difficulties could be due to any number of reasons including, but not limited to, complexities of producing batches at larger scale, equipment failure, choice and quality of raw materials and excipients, analytical testing technology, and product instability. As a result, the preclinical or clinical development of our OEC candidates could be materially delayed or we could be required to begin a new study or trial with a newly formulated drug product.

The process to generate mRNA-encoded OEC candidates encapsulated in LNPs is complex and, if not developed and manufactured under well-controlled conditions, can adversely impact pharmacological activity. Furthermore, we have not manufactured our OECs at commercial scale. We may encounter difficulties in scaling up our manufacturing process, thereby potentially impacting clinical and commercial supply.

As we continue developing manufacturing processes for our drug substance and drug product, the changes we implement to manufacturing process may in turn impact specification and stability of the drug product. Changes in our manufacturing processes may lead to failure of lots and this could lead to a substantial delay in our preclinical studies or any clinical trials. Our OEC candidates may prove to have a stability profile that leads to a lower than desired shelf life of the final approved OEC, if any. This poses risk in supply requirements, wasted stock, and higher cost of goods.

Our product and product intermediates are extremely temperature sensitive, and we may learn that any or all of our products are less stable than desired. We may also find that transportation conditions negatively impact product quality. This may require changes to the formulation or manufacturing process for one or more of our OEC candidates and result in delays or interruptions to clinical or commercial supply. In addition, the cost associated with such transportation services and the limited pool of vendors may also add additional risks of supply disruptions.

Our rate of innovation is high, which has resulted in and will continue to cause a high degree of technology change that can negatively impact product comparability during and after clinical development. Furthermore, technology changes may drive the need for changes in, modification to, or the sourcing of new manufacturing infrastructure.

***We will rely on third parties for the foreseeable future for the manufacture and supply of materials for our research programs, preclinical studies and clinical trials and we do not have long-term contracts with many of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, including drug supplies for combination therapy, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.***

Although we continue to evaluate plans to develop our own manufacturing facility, we expect to rely on third parties at least for the next several years for the manufacture of materials for our planned clinical trials and preclinical and clinical development. We expect to rely in part on third parties for commercial manufacture if any of our product candidates receive marketing approval. We do not have a long-term agreement with any of the third-party manufacturers we currently use to provide preclinical and clinical materials, and we purchase any required materials on a purchase order basis. Certain of these manufacturers are critical to our production and the loss of these manufacturers to one of our competitors or otherwise, or an inability to obtain quantities at an acceptable cost or quality, could delay, prevent, or impair our ability to timely conduct preclinical studies or clinical trials, and would materially and adversely affect our development and commercialization efforts.

We expect to continue to rely in part on third-party manufacturers for the foreseeable future for the commercial supply of any of our product candidates for which we obtain marketing approval, if any. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;

- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation or unauthorized disclosure of our intellectual property or other proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP or similar foreign regulations for manufacturing our product candidates. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain authorization for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance, and qualified personnel. If the FDA or a comparable foreign regulatory authority does not authorize these facilities for the manufacture of our product candidates or if it withdraws any such authorization in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension, or withdrawal of approvals, license revocation, seizures, or recalls of product candidates or drugs, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

***We continue to evaluate plans to acquire and establish our own manufacturing facility and infrastructure in addition to or in lieu of relying on CDMOs for the manufacture of our product candidates. Any plan to establish our own manufacturing facility and infrastructure will be costly and time-consuming, and we may not be successful.***

We may decide to lease a facility to buildout a manufacturing facility as an alternative or in addition to our reliance on CDMOs for the manufacture of drug substance for preclinical and clinical needs. If a lease is entered into, we plan to renovate and customize the manufacturing facility for our use. We expect that construction of our own manufacturing facility would provide us with enhanced control of material supply for preclinical studies and clinical trials, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in construction of a manufacturing facility and may never be successful in building our own manufacturing facility or capability. As a result, we would also need to hire additional personnel to manage our operations and facilities and develop the necessary infrastructure to continue the research and development, manufacture and eventual commercialization, if approved, of our product candidates. We, as a company, have no experience in setting up, building, or eventually managing a manufacturing facility. If we fail to select the correct location, or if we fail to enter into the lease agreement, or fail to complete the planned renovation and customization in an efficient manner, or fail to recruit the required personnel and generally manage our growth effectively, the development and production of our product candidates could be curtailed or delayed. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

In addition, the FDA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects. Problems in our manufacturing process could restrict our ability to meet clinical and market demand for our products.

We also may encounter problems hiring and retaining the experienced scientific, quality-control, and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

***We do not have experience as a company managing a manufacturing facility.***

Operating our own manufacturing facility would require significant resources, and we do not have experience as a company in managing a manufacturing facility. In part because of this lack of experience, we cannot be certain that our manufacturing plans would be completed on time, if at all, or if manufacturing of product candidates from our own manufacturing facility for our planned clinical trials will begin or be completed on time, if at all. In part because of our inexperience, we may have unacceptable or inconsistent product quality success rates and yields, and we may be unable to maintain adequate quality control, quality assurance, and qualified personnel. In addition, if we switch from our current CDMOs to our own manufacturing facility for one or more of our product candidates in the future, we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Failure to successfully obtain and operate our planned manufacturing facility could adversely affect the commercial viability of our product candidates.

***We or our third-party manufacturers may be unable to successfully scale up manufacturing of our product candidates in sufficient quality and quantity, which may impair the clinical advancement and commercialization of our product candidates.***

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we and our manufacturing partners need to manufacture them in large quantities. However, we or they may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities, as discussed above. If we, or any manufacturing partners, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of these product candidates may be delayed or infeasible, and regulatory approval or commercial launch of any resulting products may be delayed or not obtained, which could significantly harm our business. Supply sources could be interrupted from time to time and, if interrupted, it is not certain that supplies could be resumed (whether in part or in whole) within a reasonable timeframe and at an acceptable cost, or at all. If we are unable to obtain or maintain third-party manufacturing for commercial supply of our product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully.

***We have a limited number of suppliers for the lipid excipients used in our product candidates and certain of our suppliers are critical to our production. If we were to lose a critical supplier, it could have a material adverse effect on our ability to complete the development of our product candidates. If we obtain regulatory approval for any of our product candidates, we would need to expand the supply of lipid excipients in order to commercialize them.***

We have a limited number of suppliers for the lipid excipient component of our product candidates. We also do not have long-term supply agreements with all of our lipid suppliers. We may not be able to establish additional sources of supply for the lipid excipient component of our product candidates or may be unable to do so on acceptable terms.

The number of suppliers of the lipid excipients for our product candidates is limited. In the event it is necessary or desirable to acquire lipid excipients from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company, and redesign of processes can trigger the need for conducting additional studies such as comparability or bridging studies. Additionally, certain of our suppliers are critical to our production, and the loss of these suppliers to one of our competitors or otherwise would materially and adversely affect our development and commercialization efforts.

***We rely, and expect to continue to rely, on third parties to conduct certain aspects of our preclinical studies and will rely on third parties to conduct our planned clinical trials. Any failure by a third party to conduct the planned clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.***

We have relied upon and plan to continue to rely upon third parties to conduct certain aspects of our preclinical studies and will depend on third parties to conduct our planned clinical trials and to monitor and manage data for our ongoing preclinical and planned clinical programs. We rely on these parties for execution of our preclinical studies and will rely on these parties for execution of our planned clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol and legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs will be required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations or similar foreign regulations outside of the United States. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Any third parties conducting our planned clinical trials or preclinical studies are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our planned clinical trials may be extended, delayed, or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities that could harm our competitive position. In addition, principal investigators for our planned clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash and cash equivalents or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities conclude that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned, and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit to the FDA, or any comparable foreign regulatory applications we submit to foreign regulatory authorities. Any such delay or rejection could prevent us from commercializing our product candidates.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators, and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which could materially impact our ability to meet our desired preclinical and clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

***We may collaborate with third parties for the development and commercialization of our product candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.***

We may seek collaborative relationships for the development and commercialization of our product candidates. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate product revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into. Collaborations involving our product candidates pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information inappropriately or in such a way as to expose us to potential litigation or other intellectual property-related proceedings, including proceedings challenging the scope, ownership, validity, and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property rights covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and resources;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished, or terminated;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, devices, materials, know-how, or intellectual property of the collaborator relating to our product candidates;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short- and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We may face significant competition in seeking appropriate collaborations from other companies with substantially greater financial, marketing, sales, technology, or other business resources. Business combinations

among biotechnology and pharmaceutical companies have also resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate or delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us.

***Our employees and independent contractors, including principal investigators, CDMOs, CROs, consultants, vendors and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.***

Misconduct by our employees and independent contractors, including principal investigators, CDMOs, CROs, consultants, vendors, and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance, and other pharmaceutical functions and commercialization, could include intentional, reckless, or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, and other similar regulatory authorities as well as similar healthcare laws and regulations in foreign jurisdictions, including those laws that require the reporting of true, complete, and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud, and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing, and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of preclinical studies or clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal, and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight, and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

***If our CDMOs use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.***

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our manufacturers. Our manufacturers are subject to federal, state, and local laws and regulations in the United States and in the countries in which they operate governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing, and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state, or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. Generally, we do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development, and production efforts, which could harm our business, prospects, financial condition or results of operations.

## Risks Related to Intellectual Property

***If we are unable to obtain, maintain, enforce and adequately protect our intellectual property rights with respect to our technology and product candidates, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.***

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect our intellectual property and prevent others from duplicating our pipeline product candidates, or their use or manufacture, or any of and any future product candidates, and our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to such product candidates.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. Although we enter into confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, CROs, consultants, scientific advisors, and other contractors, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, and some remain so until issued. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file any patent application related to an invention or product candidate. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal, factual, and scientific questions and can be uncertain. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge the inventorship, ownership, validity, enforceability, or scope of such patents, which may result in such patents being narrowed or invalidated, or being held unenforceable. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Additionally, any U.S. provisional patent application that we file is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of filing the related provisional patent application. If we do not timely file any non-provisional patent application, we may lose our

priority date with respect to the provisional patent application and any patent protection on the inventions disclosed in the provisional patent application.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. In addition, no assurances can be given that third parties will not create similar or alternative products or methods that achieve similar results without infringing upon our patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold with respect to our programs or product candidates fail to issue, if the breadth or strength of protection of our current or future issued patents is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, or threaten our ability to commercialize our current or future product candidates. Several patent applications covering our product candidates have been filed recently by us. We cannot offer any assurances about which, if any, will result in issued patents, the breadth of any such patents or whether any issued patents will be found invalid or unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability, and our patents may be challenged in courts or patent offices in the United States and abroad. In addition, the issuance of a patent does not give us the right to practice the patented invention, as third parties may have blocking patents that could prevent us from marketing our product candidate, if approved, or practicing our own patented technology.

Wide-ranging patent reform legislation in the United States, including the Leahy-Smith America Invents Act of 2011, or the Leahy-Smith Act, may increase the uncertainty of the strength or enforceability of our intellectual property and the cost to defend it. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted and also affect patent litigation. Under the Leahy-Smith Act, the United States transitioned from a “first-to-invent” to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. This will require us to be prompt going forward during the time from invention to filing of a patent application and to be diligent in filing patent applications, but circumstances could prevent us from promptly filing or prosecuting patent applications on our inventions. The Leahy-Smith Act also enlarged the scope of disclosures that qualify as prior art. Furthermore, if a third party filed a patent application before effectiveness of applicable provisions of the Leahy-Smith Act, on March 16, 2013, an interference proceeding in the United States can be initiated by a third party to determine if it was the first to invent any of the subject matter covered by the claims of our patent applications. We may also be subject to a third party preissuance submission of prior art to the USPTO.

The Leahy-Smith Act created for the first time new procedures to challenge issued patents in the United States, including post-grant review, inter partes review and derivation proceedings, which are adversarial proceedings conducted at the USPTO, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with a priority date of March 16, 2013 or later, which all of our patent filings have, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent was filed prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of challenge, whereas inter partes review proceedings can only be brought to raise a challenge based on published prior art. These adversarial actions at the USPTO include review of patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts. The USPTO issued a final rule effective November 13, 2018 announcing that it will now use the same claim construction standard currently used in the U.S. federal courts to interpret patent claims in USPTO proceedings, which is the plain and ordinary meaning of words used. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which would result in a loss of the challenged patent right to us, including loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

As a result of all of the foregoing, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Third parties may obtain or control intellectual property rights that may prevent or limit the development of our technology or products. Third-party claims of intellectual property infringement, misappropriation or other violation may result in substantial costs or prevent or delay our development and commercialization efforts.***

Our commercial success depends in part on our avoiding actual and allegations of infringement, misappropriation or other violation of the patents and other proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, re-examination, and post-grant and inter partes review proceedings before the USPTO and similar proceedings in foreign jurisdictions, such as oppositions before the European Patent Office, or EPO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Many companies in intellectual property-dependent industries, including the pharmaceutical industry, have employed intellectual property litigation as a means to gain an advantage over their competitors. As biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to composition of matter, drug delivery, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. We cannot guarantee that our technologies, products, compositions, and their uses do not or will not infringe, misappropriate or otherwise violate third-party patent or other intellectual property rights. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. In order to successfully challenge the validity of a U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If any third-party patents were held by a court of competent jurisdiction to cover the composition of matter of any of our product candidates, the manufacturing process of any of our product candidates or the method of use for any of our product candidates, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, which may not be available at all or on commercially reasonable terms, or until such patents expire.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of the merit of such claims. We may not be aware of all intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe, misappropriate, or otherwise violate such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our

development and commercialization thereof, do not and will not infringe, misappropriate, or otherwise violate any third party's intellectual property.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates and/or harm our reputation and financial results. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could be a substantial diversion of management and employee resources from our business. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, in the case of claims concerning registered trademarks, rename our product candidates, or obtain one or more licenses from third parties, which may require substantial time and monetary expenditure, and which might be impossible or technically infeasible. Furthermore, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.***

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. For patents that are eligible for extension of patent term, we expect to seek extensions of patent terms in the United States and, if available, in other countries, however there can be no assurance that we will be granted any patent term extension we seek, or that any such patent term extension will provide us with any competitive advantage.

***If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be harmed.***

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration, and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the EU, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

***We depend on proprietary technology licensed from others. If we lose our existing licenses, we may not be able to continue developing our product candidates.***

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others.

We depend substantially on our agreements with Flagship Pioneering Innovations V, Inc., or Flagship, the Whitehead Institute for Biomedical Research, or WIBR, Acuitas Therapeutics, Inc., or Acuitas, and Nitto Denko Corporation, or Nitto, including the licenses granted thereunder. These licenses may be terminated upon certain conditions. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates.

We may also enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance, and other obligations on us. We are also obligated to achieve certain development milestones with respect to licensed products in our fields of use within specified time periods. If we fail to comply with our obligations to Flagship, WIBR, Acuitas, Nitto, or any of our other current or future licensors or collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture, or market any product candidate that is covered by these agreements, which could adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in us having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We rely on Flagship, WIBR, Acuitas, and Nitto to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over their activities or their use or licensing of any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights.

***If we are unable to obtain licenses from third parties on commercially reasonable terms or at all, or fail to comply with our obligations under such agreements, our business could be harmed.***

It is necessary for us to use the patented or other proprietary technology of third parties to commercialize our products. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license in the future, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning or otherwise controlling such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them, or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations, and prospects significantly.

Additionally, if we fail to comply with our obligations under any future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing, or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or

technology, or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

***Although we are not currently involved in any relevant litigation, we may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.***

Competitors and other third parties may infringe, misappropriate, or otherwise violate our or our future licensors' patents, trademarks, copyrights, or other intellectual property. As a result, we may need to file infringement, misappropriation, or other intellectual property-related claims against third parties. To counter infringement or other unauthorized use, we may be required to file claims on a country-by-country basis, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such claims, which often last for years before they are concluded.

Our license agreements have certain limitation on our ability to enforce the licensed patents against third party infringers. For example, with regard to our license agreements with WIBR, we cannot enforce the licensed patents against a certain third party, who previously entered into a sponsored research agreement with WIBR, with respect to inventions arising out of such sponsored research agreement. In addition, with respect to the WIBR Co-Exclusive Agreement, the WIBR patent rights are co-exclusively licensed to both us and one other third party. As such, we are not permitted to assert the co-exclusively licensed patent rights against the co-exclusive licensee.

Any claims we assert against third parties could also provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate, or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we have asserted are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

In any such proceeding, a court may decide that a patent of ours, or a patent that we in-license, is not valid, is unenforceable and/or is not infringed, or may construe such patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly or held unenforceable in whole or in part, could put our patent applications at risk of not issuing, and could limit our ability to assert those patents against those parties or other competitors and curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks, which could materially harm our business and negatively affect our position in the marketplace.

Even if we establish infringement, misappropriation, or other violation of our intellectual property, the court may decide not to grant an injunction against further such activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Weakening patent laws and enforcement by courts and other authorities in the United States and other jurisdictions may impact our ability to protect our patents.***

The U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making and other bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce and defend our existing patents and patents that we might obtain in the future.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we could become a party to foreign opposition proceedings, such as at the EPO, or patent litigation and other proceedings in a foreign court. If so, uncertainties resulting from the initiation and continuation of such proceedings could have a material adverse effect on our ability to compete in the marketplace. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

The USPTO, EPO and other patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay such fees due to non-U.S. patent agencies. While, in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors or other third parties might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We may not be able to enforce our intellectual property rights throughout the world.***

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and even in countries where we have sought protection for our intellectual property, such protection can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly developing countries, and the breadth of patent claims allowed can be inconsistent. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but where enforcement is not as strong as that in the United States or the EU. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement

for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity, or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy, and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, or other forms of intellectual property, particularly those relating to biotechnology products, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions including EU countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

***We rely on our ability to stop others from competing by enforcing our patents, however some jurisdictions may require us to grant licenses to third parties. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.***

Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties, in certain circumstances. For example, compulsory licensing, or the threat of compulsory licensing, of life-saving products and expensive products is becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Compulsory licenses could be extended to include some of our product candidates, if they receive marketing approval, which may limit our potential revenue opportunities. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may also use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products where such patent rights exist, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement if a government is the infringer, which could materially diminish the value of the patent.

***Some of our intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights and our ability to contract with non-U.S. manufacturers.***

The United States federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights". March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants" if it determines that (1) adequate steps have not been taken to commercialize the invention and achieve practical application of the government-funded technology, (2) government action is necessary to meet public health or safety needs, (3) government action is necessary to meet requirements for public use under federal regulations or (4) we fail to meet requirements of federal regulations. If the patent owner refuses to do so, the government may grant the license itself. Some of our licensed patents are subject to the provisions of the Bayh-Dole Act. If our licensors fail to comply with the regulations of the Bayh-Dole Act, they could lose title to any patents subject to such regulations, which could affect our license rights under the patents and our ability to stop others from using or commercializing similar or identical technology and products, or limit patent protection for our technology and products.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is either not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with parties who have access to them, such as our employees, CROs, consultants, scientific advisors, and other contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements, or security measures may be breached and our trade secrets could be disclosed, and we may not have adequate remedies for any such breach. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Misappropriation or unauthorized disclosure of our trade secrets or other confidential proprietary information could cause us to lose trade secret protection, impair our competitive position and have a material adverse effect on our business. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors, and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. Additionally, if the steps taken to maintain our trade secrets or other confidential proprietary information are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret or other confidential proprietary information.

Further, we cannot provide any assurances that competitors or other third parties will not otherwise gain access to our trade secrets and other confidential proprietary information or independently discover or develop substantially equivalent technology and processes. If we are unable to prevent disclosure of the trade secrets and other non-patented intellectual property related to our product candidates and technologies to third parties, there is no guarantee that we will have any such enforceable trade secret protection and we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations, and financial condition.

***We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties, that our employees have wrongfully used or disclosed alleged trade secrets of their former employers, or asserting ownership of what we regard as our own intellectual property.***

We have employed, and may in the future employ, individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of such individuals' former employers or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or our ability to hire personnel, which, in any case of the foregoing, could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Although it is our policy to require all of our employees and consultants to assign their inventions to us, to the extent that employees or consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. We may also be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Our proprietary rights may not adequately protect our technologies and product candidates, and intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of our patents;
- others, including inventors or developers of our patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing, misappropriating, or otherwise violating our intellectual property rights;
- we might not have been the first to conceive and reduce to practice the inventions covered by our patents or patent applications;
- we might not have been the first to file patent applications covering certain of our inventions;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- our pending patent applications might not result in issued patents;
- there might be prior public disclosures that could invalidate our patents;
- our issued patents may not provide us with any commercially viable products or competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors or other third parties;
- the Supreme Court of the United States, other U.S. federal courts, Congress, the USPTO or similar foreign authorities may change the standards of patentability and any such changes could narrow or invalidate, or change the scope of, our patents;
- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;

- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity, or enforceability of our patents or patent applications may be challenged by third parties; and
- the patents or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

**Risks Related to Employee Matters, Managing Growth, and Other Risks Related to Our Business**

***We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.***

We expect to experience significant growth over time in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory and clinical affairs, medical affairs, legal, finance, sales, marketing, and distribution. To manage our growth activities, we must continue to implement and improve our managerial, operational, and financial systems and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. As we expand our organization, we may have difficulty identifying, hiring, and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including:

- the need to identify, recruit, maintain, motivate, and integrate additional employees, consultants, and contractors;
- managing our internal development efforts effectively, including clinical development and regulatory review for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems, and procedures.

Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow product revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to develop and commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services, including preclinical and clinical development activities and manufacturing. There can be no assurance that the services of independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our planned clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or we are not able to effectively build out new facilities to accommodate this expansion, we may not be able to successfully implement the tasks necessary to further

develop and commercialize our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

Many of the biotechnology and pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

***If we lose our executive officers, are unable to recruit qualified officers or other key personnel, our business may materially suffer.***

We are highly dependent on our management, including our Chief Executive Officer, Mahesh Karande, our Chief Scientific Officer, Thomas McCauley, our Chief Financial Officer, Joshua Reed, and our Chief Medical Officer, Yan Moore. Due to the specialized knowledge each of our executive officers possesses with respect to our product candidates and our operations, the loss of service of any of our executive officers could delay development of our product candidates or adversely impact our business operations. We do not carry key person life insurance on any of our executive officers. In general, the employment arrangements that we have with our executive officers do not prevent them from terminating their employment with us at any time.

In addition, our future success and growth will depend in part on the continued service of our employees and management personnel and our ability to identify, hire, and retain additional personnel. Replacing key employees and management personnel may be difficult or costly and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain, or effectively incentivize key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

Many of our employees have become or will soon become vested in a substantial amount of our common stock or a number of common stock options. Our employees may be more likely to leave us if the shares they own have significantly appreciated in value relative to the original purchase prices of the shares, or if the exercise prices of the options that they hold are significantly below the market price of our common stock.

***We may engage in acquisitions or strategic collaborations that could disrupt our business, cause dilution to our stockholders, reduce our financial resources, cause us to incur debt or assume contingent liabilities, and subject us to other risks.***

In the future, we may enter into transactions to acquire other businesses, products, or technologies or enter into strategic collaborations, including licensing. If we do identify suitable acquisition or collaboration, we may not be able to complete such acquisitions or collaboration on favorable terms, or at all. Any acquisitions or collaboration we enter into may not strengthen our competitive position, and we may never realize the anticipated benefits of such acquisitions or collaborations. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business or collaboration that are not covered by the indemnification we may obtain from the seller or our collaborator. In addition, we may not be able to successfully integrate any acquired personnel, technologies, and operations into our existing business in an effective, timely, and non-disruptive manner. Acquisitions or collaborations may also divert management attention from day-to-day responsibilities, lead to a loss of key personnel, increase our expenses and reduce our cash and cash equivalents available for operations and other uses. We cannot predict the number, timing, or size of future acquisitions or collaborations or the effect that any such transactions might have on our operating results.

***The COVID-19 pandemic has impacted, and will likely continue to impact, our operations and may materially and adversely affect our business and financial results in the future.***

COVID-19 continues to spread globally. We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. The COVID-19 pandemic continues to evolve, and we cannot predict how new executive orders or other preventative measures, if any, could impact our ability to conduct our business and our product candidate development programs. Any severe disruptions in our operations as a result could negatively impact our business, results of operations, and financial condition.

In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 (and its variants) or other infectious diseases have impacted and may continue to impact our third-party service providers.

Our development efforts may be further affected by the COVID-19 pandemic, including:

- interruptions in preclinical studies due to restricted or limited operations at our or our third-party service providers' laboratory facilities, including the collection and analysis of data, or unavailability of materials;
- delays in receiving approval from regulatory authorities to initiate clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or difficulties in enrolling patients, including patients who may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services;
- delays in clinical sites receiving the supplies and materials needed to conduct clinical trials;
- diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal, state, or provincial governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical trial endpoints;
- risk that participants enrolled in clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- limitations in employee resources that would otherwise be focused on the conduct of clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- interruption in global shipping that may affect the transport of clinical trial materials or make such transport significantly more expensive;
- changes in local regulations, guidance, or practice as part of a response to the COVID-19 pandemic, which may require changes in the ways in which clinical trials are conducted or to discontinuation of clinical trials;
- delays in necessary interactions with regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- the refusal of the FDA or other comparable foreign regulatory authorities to accept data from clinical trials in geographies affected by COVID-19.

The extent to which the COVID-19 pandemic may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the effectiveness and timing of vaccines, the effectiveness of actions taken in the United States and other countries to contain and treat the disease, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, reopening plans, and the resurgence of COVID-19 or the emergence

of new strains of COVID-19. The impact to our operations due to the COVID-19 pandemic could be severe and could negatively affect our business, financial condition, and results of operations. To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risk factors described in this “Risk Factors” section.

***Litigation against us could be costly and time-consuming to defend and could result in additional liabilities.***

We may from time to time be subject to legal proceedings and claims that arise in the ordinary course of business or otherwise, such as claims brought by third parties in connection with commercial disputes and employment claims made by our current or former employees. Claims may also be asserted by or on behalf of a variety of other parties, including government agencies, patients, or stockholders.

Any litigation involving us may result in substantial costs, operationally restrict our business, and may divert management’s attention and resources, which may seriously harm our business, overall financial condition, and results of operations. Insurance may not cover existing or future claims, be sufficient to fully compensate us for one or more of such claims, or continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs, thereby adversely impacting our results of operations.

## Risks Related to Our Common Stock

***The market price of our common stock may be volatile and fluctuate substantially.***

Our stock price is likely to be volatile. As a result of this volatility, you may not be able to sell your common stock at a profit. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of our ongoing, planned, or any future preclinical studies, clinical trials, or clinical development of our product candidates or those of our competitors;
- unanticipated serious safety concerns related to the use of our product candidates;
- developments related to any future collaborations;
- developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- regulatory actions with respect to our product candidates or our competitors’ products and product candidates;
- regulatory or legal developments in the United States and other countries;
- development of third-party product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less attractive;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate a clinical trial;
- our failure to commercialize our product candidates;
- announcements by us, our collaborators or our competitors of significant acquisitions, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents, or other intellectual property or proprietary rights;
- the recruitment or departure of key scientific or management personnel;

- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- changes in accounting practices;
- the trading volume of our common stock;
- our cash and cash equivalents position;
- our ability to effectively manage our growth;
- sales of our common stock by us or our stockholders in the future;
- expiration of market stand-off or lock-up agreements;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- significant lawsuits, including intellectual property or stockholder litigation;
- the results of our efforts to engineer, develop, acquire, or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and the Nasdaq Global Select Market, or Nasdaq, and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company’s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management’s attention and resources, which would harm our business, financial condition, and results of operations.

***Our executive officers, directors, and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.***

Based on the number of shares of common stock outstanding as of December 31, 2022, our executive officers, directors, and stockholders who owned more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 71% of our outstanding voting stock. As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders would control the election of directors, the composition of our management and approval of any merger, consolidation, or sale of all or substantially all of our assets. This may prevent a change in our management or discourage unsolicited acquisition proposals or offers for our shares of common stock that you may feel are in your best interest as one of our stockholders.

***A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, holders of an aggregate of 24,284,625 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the stockholders' agreement between us and such holders. We also have registered all shares of common stock that we may issue under our equity compensation plans and these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

***We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the date of the closing of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion, subject to adjustment for inflation or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common shares that are held by non-affiliates to exceed $700 million as of the last business day of our most recently completed second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this Annual Report and intend to continue to do so in the future. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. Further, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced obligations regarding executive compensation in our periodic reports and proxy statements. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile.

***We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.***

We are considered a "smaller reporting company." We are therefore entitled to rely on certain reduced disclosure requirements for as long as we remain a smaller reporting company, such as an exemption from providing selected financial data and executive compensation information. If we qualify as a smaller reporting company because we meet the revenue limits under the definition of a smaller reporting company, we will be a "low-revenue smaller reporting company." Low-revenue smaller reporting companies are not required to obtain an

external audit on the effectiveness of their internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. These exemptions and reduced disclosures may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

***We continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company, and particularly after we are no longer an emerging growth company, we continue to incur significant legal, accounting and other expenses that we did not incur before we became a public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel are devoting a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company or a low-revenue smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm, as applicable, will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. We may discover significant deficiencies or material weaknesses in our internal control over financial reporting, which we may not successfully remediate on a timely basis or at all. Any failure to remediate any significant deficiencies or material weaknesses identified by us or to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***If we fail to maintain effective internal control over financial reporting and effective disclosure controls and procedures, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which may adversely affect investor confidence in our company.***

We are required to comply with the SEC's rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act of 2002, which require management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of our internal control over financial reporting. As an emerging growth company and a low-revenue smaller reporting company, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal

control over financial reporting pursuant to Section 404 until we are no longer an emerging growth company or a low-revenue smaller reporting company. At such time, our independent registered public accounting firm may issue a report that is adverse in the event material weaknesses have been identified in our internal control over financial reporting.

To comply with the requirements of being a public company, we have undertaken and will need to undertake additional actions, such as implementing new internal controls and procedures and hiring additional accounting or internal audit staff. Testing and maintaining internal control can divert our management's attention from other matters that are important to the operation of our business. In addition, when evaluating our internal control over financial reporting, we may identify material weaknesses that we may not be able to remediate in time to meet the applicable deadline imposed upon us for compliance with the requirements of Section 404. If we identify any material weaknesses in our internal controls over financial reporting or we are unable to comply with the requirements of Section 404 in a timely manner or assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting once we are no longer an emerging growth company, investors may lose confidence in the accuracy and completeness of our financial reports. As a result, the market price of our common stock could be materially adversely affected.

***Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.***

We are subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We are continuing to refine our disclosure controls and procedures to provide reasonable assurance that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

***If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline, even if our business is doing well.***

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We currently have limited research coverage by securities and industry analysts. If any of the analysts who cover us downgrades our common stock or issues an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***Provisions in our amended and restated certificate of incorporation and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it

more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death, or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend, or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president, or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

***Our amended and restated certificate of incorporation designates specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.***

Our amended and restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders, other than suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction and any action that the Court of Chancery of the State of Delaware has dismissed for lack of subject matter jurisdiction, which may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation also specifies that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, or the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes or federal judges experienced in resolving Securities Act disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of

discouraging lawsuits against our directors, officers, employees, and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees, or agents and result in increased costs for stockholders to bring a claim. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition, or results of operations.

***Our ability to use our net operating loss carryforwards and other tax attributes to offset future taxable income may be subject to certain limitations.***

As of December 31, 2022, we had U.S. federal and state net operating loss carryforwards, or NOLs, of $147.8 million and $143.9 million, respectively, which may be available to offset future taxable income, if any. As of December 31, 2022, we also had federal and state research and development credit carryforwards of $7.8 million and $4.0 million, respectively. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change by value in its equity ownership over a rolling three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. For these reasons, we may not be able to utilize a material portion of the NOLs or research and development credit carryforwards even if we attain profitability.

**General Risks**

***Our business and operations may suffer in the event of information technology system failures, deficiencies, or intrusions which could materially affect our results.***

Our information technology systems, as well as those of our CROs and other contractors and consultants, are vulnerable to failure or damage from computer viruses and other malware (e.g., ransomware), unauthorized access or other cybersecurity attacks, natural disasters (including hurricanes), terrorism, war, fire, and telecommunication or electrical failures. In the ordinary course of our business, we directly or indirectly collect, store, and transmit sensitive information, including intellectual property, confidential information, preclinical and clinical trial information, proprietary business information, personal information, and health-related information of our clinical trial subjects and employees, in our data centers and on our networks, or on those of third parties. The secure processing, maintenance, and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to human error (e.g., social engineering, phishing), a technical vulnerability, malfeasance, or other disruptions. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. We may not be able to anticipate all types of security threats, nor may we be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations, or hostile foreign governments or agencies. Even if we identify security incidents, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. We cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, or breaches in our systems or those of our CDMOs, CROs and other contractors and consultants.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or our critical third parties' operations, it could result in a material disruption of our product candidate development programs, our operations and ultimately, our financial results. For example, the loss of preclinical studies or clinical trial data from completed, ongoing, or planned studies or trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential, or proprietary information, we could incur liability and the further development of our product candidates could be delayed. Any such material security breach could compromise our information technology systems and the information stored there could be accessed, publicly disclosed, lost, or stolen.

Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

***We or the third parties upon whom we depend may be adversely affected by natural disasters or pandemics and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters or pandemics, other than or in addition to COVID-19, could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage, pandemic, such as the COVID-19 pandemic, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.***

The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets continue to deteriorate, or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, there is a risk that one or more of our CROs, suppliers, CDMOs, or other third-party providers may not survive an economic downturn or recession. As a result, our business, results of operations and price of our common stock may be adversely affected.

***The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.***

There has been increasing public focus by investors, patients, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, even if we are effective at addressing such concerns, we may experience increased costs as a result of executing upon our sustainability goals that may not be offset by any benefit to our reputation, which could have an adverse impact on our business and financial condition.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

***Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be your sole source of gain.***

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain all available funds and future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future.

***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

**Item 1B. Unresolved Staff Comments.**

Not Applicable.

**Item 2. Properties.**

We occupy office and laboratory space in Cambridge, Massachusetts under a shared space arrangement that expires in July 2023. In November 2021, we entered into a lease with ARE-MA Region No. 94, LLC to lease an aggregate of approximately 89,246 rentable square feet of office and laboratory space located at One Charles Park, in Cambridge, Massachusetts. The term of the lease is estimated to begin in the second quarter of 2023 and ends fifteen years after lease commencement, subject to certain extension rights. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

**Item 3. Legal Proceedings.**

We are not subject to any material legal proceedings.

**Item 4. Mine Safety Disclosures.**

Not applicable.

**INFORMATION ABOUT OUR EXECUTIVE OFFICERS AND DIRECTORS**

The following table sets forth the name, age and position of each of our executive officers and directors as of the date of this Annual Report on Form 10-K:

| Name | Age | Position |
|---|---|---|
| ***Executive Officers*** | | |
| Mahesh Karande | 50 | President, Chief Executive Officer and Director |
| Joshua Reed | 50 | Chief Financial Officer |
| Thomas McCauley, Ph.D. | 54 | Chief Scientific Officer |
| Yan Moore, M.D. | 56 | Chief Medical Officer |
| Kevin McManus | 54 | Chief Human Resources Officer |
| Ling Zeng | 54 | Chief Legal and Administrative Officer |
| ***Non-Employee Directors*** | | |
| Noubar B. Afeyan, Ph.D. | 60 | Chairman of the Board of Directors |
| Rainer Boehm | 62 | Director |
| Luke M. Beshar | 64 | Director |
| Elliott M. Levy, M.D. | 64 | Director |
| John Mendlein, Ph.D., J.D. | 63 | Director |
| Mary T. Szela | 59 | Director |
| Richard A. Young, Ph.D. | 68 | Director |

**Executive Officers**

***Mahesh Karande*** has served as the President and Chief Executive Officer and as a member of our board of directors since June 2019. From April 2018 to March 2019, Mr. Karande served as President and CEO of Macrolide Pharmaceuticals (subsequently Zikani Pharmaceuticals). From March 2010 to April 2017, Mr. Karande held senior leadership roles at Novartis, including VP and Franchise Head, US Oncology, President Novartis Africa and President Novartis Egypt. Mr. Karande holds an M.B.A. from the Wharton School, University of Pennsylvania. He is also a graduate of the Georgia Institute of Technology where he completed his M.S. in engineering and the University of Bombay where he completed his undergraduate studies in engineering. He also

currently serves on the Board of Directors of KSQ Therapeutics, a clinical-stage biotechnology company. We believe that Mr. Karande's extensive life science and leadership experience qualifies him to serve on our board of directors.

***Joshua Reed*** has served as the Chief Financial Officer since May 2022. Prior to Omega, Mr. Reed served as the Chief Financial Officer at Aldeyra Therapeutics from July 2018 to May 2022, where he was responsible for finance, business development, investor relations, compliance, human resources, and information technology. During his time at Aldeyra, Mr. Reed led multiple capital raises, oversaw the company's interactions with current and prospective investors and managed all aspects of the company's financial processes, including quarterly and annual SEC filings. Prior to Aldeyra, Mr. Reed held a variety of finance roles of increasing responsibility at Bristol-Myers Squibb, most recently serving as Vice President and Head of Finance Operations for the United States and Puerto Rico from June 2016 to July 2018. While at Bristol-Myers Squibb, Mr. Reed also led financial planning and analysis and worked on various acquisitions, divestitures, alliances, and collaboration agreements. Earlier in his career, Mr. Reed held positions at JP Morgan Chase, Credit Suisse First Boston, and Chase Manhattan Bank. He also currently serves on the Board of Directors and as Chairman of the Audit Committee of Scholar Rock, a publicly traded biotechnology company. Mr. Reed received his Bachelor of Science in Finance from Rutgers University and his Master of Business Administration from the University of Michigan's Ross School of Business.

***Thomas McCauley, Ph.D.***, has served as the Chief Scientific Officer of our company since July 2019. From September 2018 to July 2019, Dr. McCauley served as Chief Scientific Officer of Macrolide Pharmaceuticals (subsequently Zikani Therapeutics) and as Chief Scientific Officer of Translate Bio (formerly RaNA Therapeutics) from September 2016 to April 2018. From April 2010 to August 2016, Dr. McCauley served as vice president and head of Global Nonclinical Development at Shire Pharmaceuticals, where he contributed to the development and global approvals of many of Shire's products, including Replagal® for Fabry disease, Vpriv® for Gaucher disease, Elaprase® for Hunter syndrome, Firazyr® for hereditary angioedema and Xiidra® for dry eye disease. Dr. McCauley holds a Ph.D. from the University of Alabama at Birmingham and a B.S. and M.Eng. from Cornell University.

***Yan Moore, M.D.***, has served as the Chief Medical Officer of our company since January 2022. From September 2018 to December 2021, Dr. Moore served as Senior Vice President, Head of Oncology Therapeutic Area at Ipsen Pharmaceuticals. From September 2016 to September 2018, Dr. Moore was the Chief Medical Officer and Senior Vice President of Clinical Development and Research and Development at Anchiano Therapeutics (previously BioCanCell Therapeutics). Earlier in his career, Dr. Moore held various roles of increasing responsibility spanning global medical affairs and clinical development at Ariad, Sanofi, GlaxoSmithKline and Bristol Myers-Squibb. As a clinician, Dr. Moore spent time at Sapir Medical Center, Meir Hospital and Edith Wolfson Medical Center. Dr. Moore received his medical degree and Bachelor of Medical Sciences from the Sackler School of Medicine at Tel Aviv University, Master of Business Administration from the LeBow College of Business at Drexel University, and completed the Advanced Management Program at Harvard Business School.

***Kevin McManus*** has served as the Chief Human Resources Officer of our company since March 2022. From August 2019 to December 2021, Mr. McManus served as Senior Vice President and Chief Human Resources Officer at Acceleron Pharmaceuticals, where he was responsible for leading human resources, information technology and facilities functions. From April 2013 to July 2019, Mr. McManus held a variety of human resources roles of increasing responsibility at Bayer, most recently serving as Vice President and Human Resources Business Partner, Bayer Pharmaceuticals (Americas). Earlier in his career, Mr. McManus held senior human resources roles at Mylan Inc., The Ladders.com, ConvaTec, Inc., Bristol-Myers Squibb Company and GTE Corporation. Mr. McManus received his Bachelor of Science in Industrial and Labor Relations from Cornell University and Master Organization Development Practitioner from Ashridge University.

***Ling Zeng*** has served as the Chief Legal and Administrative Officer of our company since March 2022. From September 2020 to March 2022, Ms. Zeng recently served as Chief Legal Officer and Secretary at Dicerna Pharmaceuticals where she worked alongside other executives, the board of directors and their committees to develop and implement company strategy, policy, compliance, and governance activities. From August 2017 to September 2020, Ms. Zeng served as Deputy Head Legal, Group Mergers and Acquisitions, at Novartis AG, where she was responsible for global transactions across the Novartis Group, including all business units and regions. Prior to this, she served in various legal executive roles of increasing responsibility at Bausch Health Companies, Inc., Penwest Pharmaceuticals Co. and Barr Laboratories, Inc. Ms. Zeng began her legal career at

Cleary, Gottlieb, Steen and Hamilton and, prior to that, also spent time as a researcher at Alkermes Inc. and LeukoSite Inc. Ms. Zeng earned her Bachelor of Science in Physics from Peking University, Master of Science in Biophysics from Brandeis University, and her Juris Doctorate from Georgetown University.

**Non-Employee Directors**

***Noubar B. Afeyan, Ph.D.***, is a co-founder and has served as Chairman of our board of directors since 2016. In 1999, Dr. Afeyan founded Flagship Pioneering and serves as its Senior Managing Partner and Chief Executive Officer. Since 2010, Dr. Afeyan has served as Chairman of Moderna, Inc. and since 2013 has served on the board of directors of Rubius Therapeutics, Inc., both publicly traded companies. He has previously served on the boards of numerous privately and publicly held companies, including Evelo Biosciences, Inc., Kaleido Biosciences, Inc. and Seres Therapeutics, Inc. He received a Ph.D. in biochemical engineering from the Massachusetts Institute of Technology and a B.S. in chemical engineering from McGill University. Dr. Afeyan was previously a visiting lecturer of business administration at Harvard Business School and was previously a senior lecturer at MIT's Sloan School of Management where he taught courses on technology-entrepreneurship, innovation and leadership. We believe that Dr. Afeyan's significant experience co-founding, leading, and investing in numerous biotechnology companies make him qualified to serve on our board of directors.

***Rainer Boehm*** has served as a member of our board of directors since September 2022. Mr. Boehm brings over 30 years of clinical and managerial experience to Omega. He held several senior management positions during his extensive tenure at Novartis Pharma AG and its predecessor, CIBA-Geigy, spanning from 1988 to 2017, most recently as Chief Commercial & Medical Affairs Officer. He was a key figure in the successful establishment of Novartis Oncology. He oversaw the launch and life cycle management of many blockbuster brands in different geographies globally, amongst them Femara, Zometa and Glivec in oncology, as well as Cosentyx and Entresto and the immunology and cardiovascular disease areas. Prior to joining Novartis, he served as unit head at the Psychiatric Hospital in Zwiefalten, Germany. Mr. Boehm currently serves on the boards of Cellectis SA (Nasdaq: CLLS), Humanigen Inc. (Nasdaq: HGEN) and previously served on the board of Nordic Nanovector S.A. from July 2018 to April 2022. He holds a medical degree from the University of Ulm in Germany, and a Master of Business Administration from Schiller University, Strasbourg Campus in France. Recently he commenced a Master of Public Health program at the Universities of Basel / Bern / Zurich in Switzerland. We believe that Mr. Boehm's significant leadership experience in the pharmaceutical industry qualifies him to serve on our board of directors.

***Luke M. Beshar*** has served as a member of our board of directors since May 2021. Mr. Beshar has over 30 years of experience in executive leadership and chief financial officer roles principally for publicly traded and privately held pharmaceutical companies. Mr. Beshar has served as chairperson of the board of directors since January 2020 and as a member of the board of directors since October 2018 of Protara Therapeutics, a publicly traded immuno-oncology company. Mr. Beshar served on the board of directors of Trillium Therapeutics Inc., a publicly traded clinical stage immuno-oncology company from March 2014 until November 2021 when the company was acquired by Pfizer. Mr. Beshar served on the board of directors of REGENXBIO, Inc., a publicly traded leading clinical-stage gene therapy company, from May 2015 until September 2021. Previously, Mr. Beshar served as executive vice president, chief financial officer of NPS Pharmaceuticals, Inc., a publicly traded global biopharmaceutical company focused on rare diseases, from 2007 until February 2015 when the company was acquired by Shire plc. Prior to NPS Pharmaceuticals, Mr. Beshar served as executive vice president, chief financial officer of Cambrex Corporation, a publicly traded manufacturer of branded and generic active pharmaceutical ingredients and provider of related services from 2002 until 2007. Mr. Beshar began his career with Arthur Andersen & Co. and is a certified public accountant. Mr. Beshar earned his B.A. in accounting and financial administration from Michigan State University and is a graduate of The Executive Program at the Darden Graduate School of Business at the University of Virginia. We believe that Mr. Beshar's extensive leadership experience in the pharmaceutical industry qualifies him to serve on our board of directors.

***Elliott M. Levy, M.D.***, has served on our board of directors since March 2021. Dr. Levy served as Senior Vice President of Global Development of Amgen from September 2014 to June 2020 and Senior Vice President of R&D Strategy and Operations from June 2020 to May 2021. He has also served on the board of directors of NuCana plc since November 2021. Dr. Levy received his M.D. from Yale University and his B.A. from Yale College. We believe Dr. Levy's extensive experience in the industry qualifies him to serve on our board of directors.

***John Mendlein, Ph.D., J.D.***, has served as a member of our board of directors since January 2020. Dr. Mendlein currently serves as an Executive Partner at Flagship Pioneering. From January 2018 to February 2019, Dr. Mendlein served as President of Corporate and Product Strategy of Moderna, Inc. From 1996 until 2017, Dr. Mendlein held different senior executive and board roles, including Executive Chairman, Chief Executive Officer and General Counsel, of various biotechnology companies, including Affinium Pharmaceuticals (acquired by Debiopharm Group), Adnexus Therapeutics (acquired by BMS), aTyr Pharma, Inc., or aTyr, Aurora Biosciences (acquired by Vertex), and Fate Therapeutics, Inc., or Fate. From 2011 to 2017, he also served as Chief Executive Officer of aTyr. He started his biotechnology career at Smith Kline and French (now GlaxoSmithKline). He currently serves as Vice Chairman of the board of directors of Fate and previously served on the public boards of directors of Moderna, Monogram, aTyr, and Editas Medicine, Inc. Dr. Mendlein holds a Ph.D. in physiology and biophysics from the University of California, Los Angeles, a J.D. from the University of California, Hastings College of the Law, and a B.S. in biology from the University of Miami. We believe that Dr. Mendlein's extensive scientific experience and experience in the biotechnology industry qualifies him to serve on our board of directors.

***Mary T. Szela*** has served as a member of our board of directors since June 2019. Ms. Szela currently serves as the Chief Executive Officer and President of TriSalus Life Sciences, Inc. (formerly Surefire Medical, Inc.), a privately held immuno-oncology company. From January 2016 to November 2016, Ms. Szela served as Chief Executive Officer and a director of Aegerion Pharmaceuticals, Inc. In November 2016, Aegerion Pharmaceuticals, Inc. merged with QLT Inc. to form Novelion Therapeutics Inc. where Ms. Szela served as Chief Executive Officer and as a member of its board of directors until November 2017. Ms. Szela served as the Chief Executive Officer and a member of the board of directors of Melinta Therapeutics, Inc., an antibiotic development company, from April 2013 to August 2015. Ms. Szela held ascending management positions at Abbott Laboratories from 1987 to 2012, including President of the company's U.S. pharmaceutical business from January 2008 to December 2010. Ms. Szela has served as a member of the public boards of directors of Kura Oncology, Inc. since November 2018, Prometheus Biosciences since March 2021, Coherus Biosciences from July 2014 to August 2021 and Alimera Sciences Inc. from June 2018 to March 2021. Ms. Szela has also served as a member of the board of directors of TriSalus Life Sciences, Inc., a privately held company, since January 2018. She also previously served as a member of the board of directors Receptos, Inc. from June 2014 to July 2015, Novo Nordisk from March 2014 to March 2017, and Macrolide Pharmaceuticals, from March 2018 to July 2019. Ms. Szela earned an M.B.A. in Business and a B.S. in nursing, both from the University of Illinois. We believe that Ms. Szela's extensive leadership experience in the pharmaceutical industry qualifies her to serve on our board of directors.

***Richard A. Young, Ph.D.***, has served on our board of directors since August 2017. He has been a member of the Whitehead Institute and Professor of Biology at the Massachusetts Institute of Technology since 1984. Dr. Young currently serves as a member of the board of directors of Syros Pharmaceuticals, Inc. since November 2011. In May 2012, he was elected to the National Academy of Sciences and in October of 2019, he was elected to the National Academy of Medicine. Dr. Young received his Ph.D. in molecular biophysics and biochemistry from Yale University. We believe Dr. Young is qualified to serve on our board of directors because of his scientific expertise.

## PART II

### Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

***Market information***

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "OMGA" since July 30, 2021. Prior to that time, there was no public market for our common stock.

***Holders***

As of February 24, 2023, there were approximately 79 holders of record of our common stock. The actual number of stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

***Dividend Policy***

We have never declared or paid any cash dividends on our common stock since our inception. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

**Recent sales of unregistered securities**

We did not make any sales of unregistered securities during the year ended December 31, 2022.

**Use of proceeds from registered securities**

On August 3, 2021, we completed our initial public offering ("IPO"). The offer and sale of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-257794), which was declared effective on July 29, 2021.

The net proceeds of approximately $128.1 million from our IPO have been invested in capital preservation investments, which include interest bearing savings accounts, short-term and intermediate-term, investment-grade securities, interest-bearing instruments and U.S. government securities. Information related to our intended use of the proceeds from our IPO is included in the "Use of Proceeds" section of our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on August 2, 2021, and there has been no material change in our planned use of the balance of the net proceeds from our IPO described in such prospectus.

### Item 6. [Reserved]

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.**

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis. Please also see the "Special Note Regarding Forward-Looking Statements" section of this Annual Report on Form 10-K.*

## Overview

Omega Therapeutics is a clinical-stage biotechnology company pioneering a new class of programmable epigenetic mRNA medicines. Our OMEGA platform harnesses the power of epigenetics and our deep understanding of genomic architecture to precisely target and controllably modulate gene expression at the pre-transcriptional level to treat or cure diseases. We have deciphered the three-dimensional architecture of the human genome. Genes and their accompanying regulators are organized into distinct and evolutionarily conserved structures called Insulated Genomic Domains, or IGDs. IGDs are the fundamental structural and functional units of gene control and cell differentiation and act as nature's "control room" of biology. Most diseases are caused by aberrant gene expression rooted in alterations in IGDs. The OMEGA platform has enabled us to systematically identify and validate thousands of novel DNA-sequence-based epigenomic "zip codes" associated with individual regulatory elements within IGDs. We call these epigenomic targets EpiZips. We rationally design and engineer our mRNA therapeutics, which are programmable and modular epigenetic medicines, called Omega Epigenomic Controllers, or OECs, to target EpiZips for Precision Epigenomic Control. This enables us to precisely tune genes to a desired level of expression and to control the duration of expression. Through this approach, we believe that the OMEGA platform has broad potential applicability across a range of diseases and conditions. Our pipeline currently consists of early-stage programs that span oncology, multigenic diseases including immunology, regenerative medicine, and select monogenic diseases.

Since our inception, we have incurred significant operating losses. We have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our preclinical development activities and preparing for and initiating clinical trials of our product candidates. To date, we have funded our operations primarily with proceeds from sales of equity securities and borrowings under our loan and security agreement.

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $124.7 million. In August 2021, we completed our initial public offering ("IPO") pursuant to which we issued and sold 8,300,976 shares of our common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. We received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us.

Our ability to generate product revenue will depend on the successful development, regulatory approval, and eventual commercialization of one or more of our product candidates. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Additional sources of financing might not be available to us on favorable terms, if at all. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance product candidates through clinical development, continue preclinical development, expand our research and development activities, develop new product candidates, complete preclinical studies and clinical

trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. Our expenses will also increase substantially if or as we:

- continue our research and development efforts and submit INDs for our product candidates;
- initiate and conduct clinical trials of our product candidates;
- continue to engineer and develop additional product candidates;
- continue to develop the OMEGA platform;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish manufacturing and supply chain capacity sufficient to provide clinical and, if applicable, commercial quantities of product candidates, including building our own manufacturing facility;
- establish a sales, marketing, internal systems and distribution infrastructure to commercialize any products for which we may obtain regulatory approval, if any, in geographies in which we plan to commercialize our products ourselves;
- maintain, expand, protect and enforce our intellectual property estate;
- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan and support our product development and potential future commercialization efforts;
- enter into collaborations or licenses for new technologies;
- make royalty, milestone, or other payments under our current and any future in-license agreements;
- incur additional legal, accounting, and other expenses in operating our business; and
- continue to operate as a public company.

**Recent Developments**

In October 2022, we entered into a Collaboration and License Agreement with Nitto Denko Corporation, pursuant to which, Nitto granted us an exclusive, worldwide, royalty-bearing, fully transferable and fully sublicensable license under all intellectual property (the “Licensed IP”) owned or controlled by Nitto relating to its lipid nanoparticle (“LNP”) delivery technology that is necessary or useful to research, develop, commercialize, make, have made, use, sell, have sold, offer for sale, or import any product (a “Licensed Product”) directed to the c-Myc oncogene in lung that (a) consists of (i) one LNP composition approved by a joint steering committee established by us and Nitto and (ii) one or more epigenomic controllers controlled by us and (b) (i) but for the licenses granted to us by Nitto, would infringe at least one valid claim in the Licensed IP or (ii) incorporates or otherwise makes use of the data, results or know-how included in the Licensed IP.

**Development Programs**

*OTX-2002*

In July 2022, we announced clearance of our investigational new drug (“IND”) application from the United States Food and Drug Administration ("FDA") to initiate a Phase 1/2, first-in-human, clinical trial of OTX-2002 for the treatment of hepatocellular carcinoma, or HCC.

The MYCHELANGELO™ I clinical trial has initiated and in October 2022 we announced that the first patient had been dosed. The Phase 1/2 MYCHELANGELO I trial will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of OTX-2002 as a monotherapy (Part 1) and in combination with standard of care therapies (Part 2) 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 up to 190 patients at clinical trial sites in the United States, Asia, and Europe.

In November 2022, we announced that OTX-2002 was granted Orphan Drug Designation by the FDA for the treatment of HCC.

*OTX-2101*

In October 2022, we announced the selection of OTX-2101 as the second OEC development candidate to advance into IND-enabling studies for the treatment of non-small cell lung cancer, or NSCLC.

*Other OEC programs*

Beyond HCC and NSCLC, we continue to advance multiple OECs from the OMEGA platform through preclinical studies. The CXCL 1-8-targeting OEC has been characterized in preclinical studies and has potential in several indications including neutrophilic asthma, acute respiratory distress syndrome (including COVID-related), dermatological and rheumatological indications, and oncology, representing a potential franchise opportunity.

**Impact of COVID-19 on our business**

The worldwide COVID-19 pandemic, including the identification of new variants of the virus, may affect our ability to initiate and complete preclinical studies, delay the initiation and completion of our clinical trials, or have other adverse effects on our business, results of operations, financial condition, and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could adversely affect our business, operations and ability to raise funds to support our operations.

To date, we have not experienced material business disruptions as a result of the pandemic. We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. The third-party contract research organizations, or CROs, and contract development and manufacturing organizations, or CDMOs, that we engage have faced in the past and may face in the future disruptions that could affect our ability to initiate and complete preclinical studies, including disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates and laboratory supplies for our preclinical studies, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic.

We cannot be certain what the overall impact of the COVID-19 pandemic, or the variants of the virus, will be on our business, and the pandemic has the potential to adversely affect our business, financial condition, results of operations, and prospects.

**Components of our results of operations**

***Revenue***

To date, we have not generated any revenue from product sales, and do not expect to generate any revenue from the sale of products for the foreseeable future. Our revenue to date has been generated through our collaboration agreement with PM (CF) Explorations, Inc., or PMCo, an affiliate of Flagship Pioneering (“Flagship”), in which we are entitled to receive reimbursement for the costs associated with our research activities performed.

***Operating expenses***

*Research and development expenses*

Research and development expenses consist primarily of costs incurred in performing research and development activities, which include:

- personnel-related expenses, including salaries, bonuses, benefits, and stock-based compensation for employees engaged in research and development functions;
- expenses incurred in connection with the discovery, preclinical development, and clinical development of our research programs, including under agreements with third parties, such as

consultants, contractors, CROs and CDMOs that manufacture material for use in our discovery, preclinical development, and clinical development;

- laboratory supplies and research materials;
- costs of licensing technology; and
- facilities, depreciation, and other expenses which include direct and allocated expenses.

We expense research and development costs as incurred. Costs for research and development activities are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

We do not allocate costs associated with our discovery efforts, laboratory supplies and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and the OMEGA platform. We use internal resources primarily to conduct our research and discovery activities as well as for managing our preclinical development, process development, manufacturing and clinical development activities. These employees work across multiple programs and our technology platform and, therefore, we do not track these costs by program.

We expect that our research and development expenses will continue to increase as we continue our current discovery and research programs, initiate new research programs, continue preclinical development of our product candidates and conduct clinical trials for OTX-2002 and any of our other product candidates.

*General and administrative expenses*

General and administrative expenses consist primarily of salaries and other related costs such as bonuses and benefits, including stock-based compensation, for personnel in our executive, finance, legal, human resources, corporate business development, and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, information technology, auditing, tax, consulting services, insurance and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also expect to continue to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory, and tax compliance services, directors' and officers' liability insurance costs, and investor and public relations costs.

*Related party expense, net*

Related party expense, net consists primarily of fees paid to Flagship for reimbursement of certain expenses, including insurance and benefits, general consulting, and software licenses incurred on our behalf. Additionally, our principal office and laboratory space is leased with an affiliate of Flagship, and we also sublease our other office and laboratory space to two other parties which are affiliates of Flagship. The rent expense and costs related to our principal office and laboratory space, including real estate taxes, insurance, and normal maintenance costs, are considered as related party expenses. Such related party expenses are offset with sublease income received from our related parties, which is comprised of base rent and costs related to the subleased premises such as real estate taxes, cost of operations, maintenance, repair, replacement, and property management.

***Other income (expense), net***

*Interest income (expense), net*

Interest expense primarily consists of interest payments as well as the amortization of the debt discount related to our loan and security agreement. Interest income primarily consists of interest earned on corporate debt securities.

*Other expense, net*

Other expense, net primarily consists of foreign exchange gains and losses on invoices paid, as well as remeasurement gains and losses associated with changes in the fair value of the warrant liability and the success fee obligation related to our loan and security agreement, as amended. Until settlement, fluctuations in the fair value of our warrant liability and success fee obligation are based on the remeasurement at each reporting period.

**Results of operations**

***Comparison for the years ended December 31, 2022 and 2021***

The following table summarizes the results of our operations for the years ended December 31, 2022 and 2021, together with the changes in those items in thousands of dollars and as a percentage.

| | Year Ended December 31, | | $ Increase / (Decrease) | % Change |
|---|---|---|---|---|
| | 2022 | 2021 | | |
| Collaboration revenue from related party | $ 2,073 | $ 144 | $ 1,929 | 100 % |
| Operating expenses: | | | | |
| Research and development | 79,996 | 47,865 | 32,131 | 67 % |
| General and administrative | 21,821 | 16,603 | 5,218 | 31 % |
| Related party expense, net | 3,022 | 1,708 | 1,314 | 77 % |
| Total operating expenses | 104,839 | 66,176 | 38,663 | 58 % |
| Loss from operations | (102,766) | (66,032) | 36,734 | 56 % |
| Other income (expense), net: | | | | |
| Interest income (expense), net | 222 | (910) | (1,132) | (124)% |
| Change in fair value of warrant liability | — | (1,310) | (1,310) | (100)% |
| Other expense, net | (157) | (28) | 129 | NM |
| Total other income (expense), net | 65 | (2,248) | (2,313) | (103)% |
| Net loss | $ (102,701) | $ (68,280) | $ 34,421 | |

NM - Not meaningful

*Revenue*

Revenue increased by $1.9 million to $2.1 million for the year ended December 31, 2022, from $0.1 million for the year ended December 31, 2021. The $1.9 million increase was due to a full year of collaboration revenue recognized in 2022 for reimbursement of research costs incurred in connection with the collaboration agreement with PMCo. The agreement was entered into in November 2021.

*Research and development expenses*

Research and development expenses increased by $32.1 million to $80.0 million for the year ended December 31, 2022, from $47.9 million for the year ended December 31, 2021. The $32.1 million increase was primarily driven by an increase of $12.1 million in personnel-related expenses, including stock-based compensation to support business growth, an increase of $12.2 million in external manufacturing costs and study costs in support of the advancement of our programs, an increase of $4.3 million attributable to clinical development costs, an increase of $2.2 million primarily attributable to facilities and overhead expenses, and the remaining increase of $1.3 million in costs of licensing technology.

*General and administrative expenses*

General and administrative expenses increased by $5.2 million to $21.8 million for the year ended December 31, 2022, from $16.6 million for the year ended December 31, 2021. The $5.2 million increase was primarily driven by an increase of $4.0 million in personnel-related expenses, including stock-based compensation to support business growth, an increase of $1.1 million in directors' and officers' liability insurance, with the remaining $0.1 million increase primarily attributable to higher professional fees and consulting services associated with ongoing business activities.

*Related party expense, net*

Related party expense, net was $3.0 million for the year ended December 31, 2022 and $1.7 million for the year ended December 31, 2021. The $1.3 million increase was primarily driven by an increase in lease expense and related costs incurred for our principal office and laboratory space, an increase in benefits expenses payable to Flagship due to company growth, and an increase in board fees paid to our non-employee directors due to a full year of board fees paid in 2022 versus five months in 2021.

*Interest income (expense), net*

Interest income (expense), net was $0.2 million of income for the year ended December 31, 2022 and $0.9 million of expense for the year ended December 31, 2021. The $1.1 million increase in interest income, net was attributed to an increase in interest income earned on corporate debt securities during the year ended December 31, 2022.

*Change in fair value of warrant liability*

During the year ended December 31, 2021, there was $1.3 million incurred related to the change in fair value of warrant liability. Upon the closing of the IPO, the warrants for the purchase of preferred stock automatically became warrants for the purchase of common stock, and we reclassified the carrying value of the warrants from liability to additional paid-in capital on our balance sheet. In August 2021, the holders of such warrants completed a cashless exercise of the warrants, and we issued 82,193 shares of our common stock. No changes in fair value of warrant liabilities were recorded for the year ended December 31, 2022.

*Other expense, net*

Other expense, net was $0.2 million for the year ended December 31, 2022 and less than $0.1 million for the year ended December 31, 2021.

**Liquidity and capital resources**

*Sources of liquidity*

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we support our continued research activities and development of our programs and platform. We have not yet commercialized any products, and we do not expect to generate product revenue for several years, if at all. To date, we have funded our operations primarily with proceeds from sales of equity securities, including our IPO, and borrowings under our loan and security agreement.

In August 2021, we completed our IPO pursuant to which we issued and sold 8,300,976 shares of our common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. We received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us.

*Cash flows*

The following table summarizes our sources and uses of cash for each of the periods presented (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Net cash used in operating activities | $ (98,515) | $ (57,609) |
| Net cash used in investing activities | (18,060) | (40,399) |
| Net cash provided by financing activities | 708 | 261,539 |
| Net change in cash, cash equivalents, and restricted cash | $ (115,867) | $ 163,531 |

*Operating activities*

Net cash used in operating activities totaled $98.5 million for the year ended December 31, 2022 compared to net cash used in operating activities of $57.6 million for the year ended December 31, 2021. The $40.9 million increase in operating cash outflows was primarily attributable to $34.4 million higher net loss recognized during the year ended December 31, 2022 and higher cash outflows due to changes in operating assets and liabilities, offset by higher non-cash charges including stock-based compensation and amortization of right-of-use assets.

*Investing activities*

Net cash used in investing activities totaled $18.1 million for the year ended December 31, 2022 compared to net cash used in investing activities of $40.4 million for the year ended December 31, 2021. The decrease was attributable to proceeds received from maturities of marketable securities in 2022.

*Financing activities*

Net cash provided by financing activities for the year ended December 31, 2022 consisted primarily of the proceeds from the exercise of stock options. Net cash provided by financing activities for the year ended December 31, 2021 consisted primarily of the proceeds from our IPO of $128.1 million, net of underwriting discounts and payments for offering costs, and net proceeds from the issuance of Series C redeemable convertible preferred stock of $125.4 million in March 2021.

***Loan and security agreement***

In March 2018, we entered into the loan and security agreement, or Loan Agreement, with Pacific Western Bank, or PWB, under which we borrowed $8.0 million. In September 2019, we entered into an amendment to the Loan Agreement, or First Amendment, in which PWB made an additional term loan to us in an aggregate principal amount of $12.0 million. The Loan Agreement was further amended in December 2020 to extend the principal repayment date.

In December 2021, we entered into an amendment to the Loan Agreement, or Fourth Amendment, in which PWB made an additional term loan to us in an aggregate principal amount of $20.0 million. The proceeds of the Fourth Amendment were first applied to the repayment in full of all outstanding principal and accrued interest on the then outstanding term loan of $12.0 million, and the remaining cash proceeds of $8.0 million were used for general working capital and for capital expenditures purposes. The maturity date of the additional term loan is September 30, 2025, and it will be repaid beginning on September 30, 2023 in twenty-four equal monthly installments, including interest at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%, due monthly starting the first month after December 20, 2021. As of December 31, 2022, the interest rate applicable to the term loan was 8.0% and the interest payment on the outstanding term loan was less than $0.1 million per month.

Borrowings under the Loan Agreement, as amended, are collateralized by substantially all of our personal property, other than our intellectual property. There are no financial covenants associated with the Loan Agreement, as amended; however, we are subject to certain affirmative and negative covenants to which we will remain subject to until maturity.

***Funding requirements***

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $124.7 million. We expect that our expenses will increase substantially in connection with our ongoing activities, particularly as we advance preclinical activities and conduct clinical trials for OTX-2002 and any other product candidates in

development. In addition, we will continue to incur additional costs associated with operating as a public company. The timing and amount of our operating and capital expenditures will depend largely on:

- the scope, progress, results, and costs of our preclinical studies, and clinical trials of OTX-2002 and any future clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for our current and future product candidates in regions where we choose to commercialize any products;
- the number of future product candidates and potential additional indications that we may pursue and their development requirements;
- the stability, scale, yield, and cost of our manufacturing process as we scale-up production and formulation of our product candidates for clinical trials, in preparation for regulatory approval and in preparation for commercialization, including our ability to build our own manufacturing facility;
- the costs of pre- and post-commercialization activities for any approved product, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- the costs and timing of changes in pharmaceutical pricing and reimbursement infrastructure;
- the costs and timing of changes in the regulatory environment and enforcement rules;
- our ability to compete with other therapeutics in the indications we target;
- the effect of competing technological and market developments;
- the extent to which we enter into collaborations or licenses for products, product candidates, or technologies;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs of preparing, filing, and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims;
- the costs of operating as a public company; and
- the severity, duration, and impact of the COVID-19 pandemic, which may adversely impact our business.

We believe that our existing cash, cash equivalents and marketable securities, together with the net proceeds from the registered direct offering completed on February 27, 2023, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2024. We have based this estimate on assumptions that may prove to be incorrect, and we could utilize our available capital resources sooner than we expect. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources.

**Contractual obligations**

We enter into contracts in the normal course of business with CROs, CDMOs, and other third parties for preclinical research studies and testing and manufacturing services. These contracts typically do not contain minimum purchase commitments and are generally cancelable by us upon written notice. Payments due upon cancellation consist of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation and in the case of certain arrangements with CROs and CDMOs may include non-cancelable fees. The amount and timing of cancellation payments are not known until such time a contract is canceled.

We have also entered into license agreements with Flagship Pioneering Innovations V, Inc., Whitehead Institute for Biomedical Research, Acuitas and Nitto Denko Corporation, under which we are obligated to make

potential milestone payments, royalty payments, or both. Such payments are dependent upon the development of products using the intellectual property licensed under the agreements and are contingent upon the occurrence of future events; as such, the timing and likelihood of such potential obligations are not known with certainty.

As described previously, we borrowed an aggregate principal amount of $20.0 million under the Loan Agreement, as amended. Pursuant to the terms of the Loan Agreement, as amended, interest payment on the outstanding term loan is less than $0.1 million per month, and we are obligated to repay $0.8 million of principal payment per month, beginning on September 30, 2023 until the maturity date of September 30, 2025.

In July 2020, we entered into a Shared Space Agreement with an affiliate of Flagship for our principal office and laboratory space. The Shared Space Arrangement commenced on August 1, 2020 and continues through July 31, 2022 with two options to extend the term for a period of 24 months each. In January 2022, we entered into an amendment to modify certain terms of the Shared Space Agreement and exercise the option to renew the lease term for another 12 months. The lease term will now expire in July 2023. In connection with the modifications in the amendment, we paid an upfront payment of $2.9 million in the first quarter of 2022, which will cover the rent payments for the extended lease term.

We also have another office and laboratory space which is under a noncancelable lease agreement entered in 2017 and will expire in September 2024. Our lease payments for the remainder of the lease term will be approximately $0.1 million per month. In September 2020, the space was fully subleased to two other parties, which are affiliates of Flagship. One of the sublease agreements terminated in May 2022, and the other sublease agreement expires in September 2024.

In November 2021, we entered into a lease with ARE-MA Region No. 94, LLC to lease an aggregate of approximately 89,246 rentable square feet of office and laboratory space located at One Charles Park, Cambridge, Massachusetts, 02142. The term of the Lease is estimated to begin in the second quarter of 2023 and ends fifteen years after lease commencement, subject to certain extension rights. The base rent for the leased space will be $115.00 per square foot, subject to an annual upward adjustment of 3% of the then current rental rate, starting on the first anniversary of the first payment of rent under the lease, and other potential adjustments based on our utilization of certain tenant improvement allowances. We intend to sublease a portion of this facility to supplement our growth plan.

## Critical accounting policies and estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S., or GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses. On an ongoing basis, we evaluate these estimates and judgments, including those described below. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results and experiences may differ materially from these estimates.

While our significant accounting policies are more fully described in Note 2 - Summary of Significant Accounting Policies in the Notes to consolidated financial statements appearing at the end of this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

### *Accrued research and development expenses*

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically

confirm the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to vendors in connection with preclinical and clinical development activities, CROs in connection with clinical development and research activities, and CDMOs in connection with the production of research materials.

We estimate accrued research and development expenses based on our estimates of the services received and efforts expended pursuant to quotes and contracts with third-party service providers, including CROs and CDMOs that supply, conduct and manage preclinical and clinical studies our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense, in which it will be evaluated for current or long-term classification based on when it is expected to be realized. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in changes in estimates that increase or decrease amounts recognized in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

***Stock-based compensation***

We recognize all stock-based compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award, based on their fair values. Forfeitures are recognized as they occur. For stock option awards, the Company estimates the fair value on the date of the grant using the Black-Scholes option pricing model with the following inputs: (1) fair value of our common stock, (2) assumptions we make for the expected volatility of our common stock, (3) the expected term of our stock option awards, (4) the risk-free interest rate for a period that approximates the expected term of our stock option awards, and (5) our expected dividend yield, if any. Prior to our IPO in August 2021, there was no public market for our common stock. As a result, prior to our IPO, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believes are relevant and which may have changed from the date of the most recent valuation through the date of the grant. Following our IPO, the fair value of our common stock is determined based on the quoted market price of our common stock. Additionally, due to the continued lack of sufficient company-specific historical and implied volatility data, we have based our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development and life science industry focus.

The assumptions included in the Black-Scholes option pricing model significantly affect our stock option valuations, and future changes in these assumptions could significantly change valuations of future stock option grants and, thus, affect future stock-based compensation expense. In addition, if circumstances were to change such that we determined stock options values were better represented by an alternative valuation method, such change could also significantly affect future stock-based compensation expense. To date, there have not been any material adjustments to our prior estimates included in the Black-Scholes option pricing model.

**Recently Issued Accounting Pronouncements**

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases. The Company adopted ASU 2016-02, and related amendments, on January 1, 2022. A description of this adoption is disclosed in Note 2 - Summary of Significant Accounting Policies in the Notes to consolidated financial statements appearing at the end of this Annual Report.

**Emerging growth company and smaller reporting company status**

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As a result, we may take advantage of specified reduced disclosure and other reporting requirements that are otherwise applicable generally to public companies. In particular, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we may adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company.

We are also a “smaller reporting company” as defined under the Securities Act and Exchange Act. We may continue to be a smaller reporting company so long as either (i) the market value of shares of our common stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of shares of our common stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation, and, similar to emerging growth companies, if we are a smaller reporting company under the requirements of (ii) above, we would not be required to obtain an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

**Item 7A. Quantitative and Qualitative Disclosures About Market Risk.**

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 7A.

**Item 8. Financial Statements and Supplementary Data.**

The financial information required by Item 8 is located beginning on page F-1 of this report.

**Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.**

None.

**Item 9A. Controls and Procedures.**

*Limitations on effectiveness of controls and procedures*

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints, and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

*Evaluation of disclosure controls and procedures*

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of December 31, 2022, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on the evaluation, our principal executive officer and principal financial officer concluded that, as of December 31, 2022, our disclosure controls and procedures as of such date are effective at the reasonable assurance level.

*Management's annual report on internal control over financial reporting*

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies".

*Changes in Internal Control over Financial Reporting*

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information.**

None.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.**

Not applicable.

## PART III

### Item 10. Directors, Executive Officers and Corporate Governance.

**Code of Business Conduct and Ethics**

We have adopted a written code of business conduct and ethics, or Code, which applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the Code is available on the investor section of our website at ir.omegatherapeutics.com. We intend to disclose on our website any amendments to, or waivers from, our Code that are required to be disclosed pursuant to SEC or Nasdaq rules. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this Annual Report on Form 10-K.

**Executive Officers and Directors**

The information concerning our executive officers and directors required by this Item 10 is contained under the caption “Information about our Executive Officers and Directors” at the end of Part I of this Annual Report on Form 10-K.

The remainder of the information required by this Item 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2023 Annual Meeting of Stockholders under the headings “Corporate Governance,” “Delinquent Section 16(a) Reports” (if applicable) and “Committees of the Board” and is incorporated herein by reference.

### Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders under the headings “Executive and Director Compensation” and “Compensation Committee Interlocks and Insider Participation” (if applicable) and is incorporated herein by reference.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.**

**Securities Authorized for Issuance Under Equity Compensation Plans (as of December 31, 2022)**

| Plan Category | Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights | Weighted Average Exercise Price of Outstanding Options, Warrants and Rights | Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities in first column) |
|---|---|---|---|
| Equity compensation plans approved by security holders[1] | 8,438,573[2] | $ 8.40[3] | 2,110,286[4] |
| Equity compensation plans not approved by security holders | — | — | — |
| Total | 8,438,573 | | 2,110,286 |

(1) Consists of the Omega Therapeutics, Inc. 2017 Equity Incentive Plan, as amended (the "2017 Plan"), the Omega Therapeutics, Inc. 2021 Incentive Award Plan (the "2021 Plan") and the Omega Therapeutics, Inc. 2021 Employee Stock Purchase Plan (the "2021 ESPP").

(2) Includes 4,069,183 outstanding options to purchase stock under the 2017 Plan and 4,369,390 outstanding options to purchase stock under the 2021 Plan.

(3) As of December 31, 2022, the weighted average exercise price of outstanding options under the 2017 Plan was $3.14 and the weighted average exercise price of outstanding options under the 2021 Plan was $8.67.

(4) Includes 1,152,352 shares available for future issuance under the 2021 Plan and 957,934 shares available for issuance under the 2021 ESPP. As of July 29, 2021, in connection with our initial public offering, no further grants are made under the 2017 Plan. The 2021 Plan provides for an annual increase to the number of shares available for issuance thereunder on the first day of each calendar year beginning on January 1, 2022 and ending on and including January 1, 2031, by an amount equal to the lesser of (i) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by our board of directors (but no more than 26,810,000 shares may be issued upon the exercise of incentive stock options). The 2021 ESPP provides for an annual increase to the number of shares available for issuance thereunder on the first day of each calendar year beginning on January 1, 2022 and ending on and including January 1, 2031, by an amount equal to the lesser of (i) 1% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by our board of directors, provided that no more than 6,450,000 shares of our common stock may be issued under the 2021 ESPP.

The remainder of the information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders under the heading "Security Ownership of Certain Beneficial Owners and Management" and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence.**

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders under the headings "Corporate Governance" and "Certain Relationships and Related Person Transactions" and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services.**

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders under the heading “Independent Registered Public Accounting Firm Fees and Other Matters” and is incorporated herein by reference.

**PART IV**

**Item 15. Exhibits, Financial Statement Schedules.**

(a)(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(a)(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(a)(3) Exhibits:

| Exhibit Number | Description | Incorporated by Reference | | | Filing Date | Filed/ Furnished Herewith |
|---|---|---|---|---|---|---|
| | | Form | File No. | Exhibit | | |
| 3.1 | Restated Certificate of Incorporation. | 8-K | 001-40657 | 3.1 | 08/03/2021 | |
| 3.2 | Amended and Restated Bylaws. | 8-K | 001-40657 | 3.2 | 08/03/2021 | |
| 4.1 | Specimen Certificate of Common Stock. | S-1/A | 333-257794 | 4.2 | 07/26/2021 | |
| 4.2 | Amended and Restated Investor Rights' Agreement, dated March 4, 2021. | S-1/A | 333-257794 | 4.1 | 07/26/2021 | |
| 4.3 | Amended and Restated Warrant to Purchase Stock issued to PacWest Bankcorp, dated September 30, 2019, to purchase Series A preferred stock. | S-1/A | 333-257794 | 4.3 | 07/26/2021 | |
| 4.4 | Description of Capital Stock. | 10-K | 001-40657 | 4.4 | 03/10/2022 | |
| 10.1# | Form of Indemnification Agreement between Omega Therapeutics, Inc. and its directors and officers. | S-1/A | 333-257794 | 10.8 | 7/26/2021 | |
| 10.2# | 2021 Incentive Award Plan and form of agreements thereunder. | S-1/A | 333-257794 | 10.2 | 7/26/2021 | |
| 10.3# | 2021 Employee Stock Purchase Plan. | S-1/A | 333-257794 | 10.3 | 7/26/2021 | |
| 10.4# | Non-Employee Director Compensation Program. | S-1/A | 333-257794 | 10.4 | 7/26/2021 | |
| 10.5# | Employment Agreement by and between Mahesh Karande and the Registrant, dated July 25, 2021. | S-1/A | 333-257794 | 10.17 | 7/26/2021 | |
| 10.6# | Employment Agreement by and between Thomas McCauley and the Registrant, dated July 24, 2021. | S-1/A | 333-257794 | 10.18 | 7/26/2021 | |
| 10.7# | Employment Agreement by and between Yan Moore and the Registrant, dated December 12, 2021. | 10-K | 001-40657 | 10.8 | 3/10/2022 | |
| 10.8# | Employment Agreement by and between Kevin McManus and the Registrant, dated February 3, 2022. | 10-Q | 001-40657 | 10.2 | 05/04/2022 | |
| 10.9# | Employment Agreement by and between Ling Zeng and the Registrant, dated March 18, 2022. | 10-Q | 001-40657 | 10.3 | 05/04/2022 | |
| 10.10# | Employment Agreement by and between Joshua Reed and the Registrant, dated April 28, 2022. | 10-Q | 001-40657 | 10.4 | 05/04/2022 | |
| 10.11# | Consulting Agreement by and between Richard A. Young and the Registrant, dated November 7, 2016. | 10-K | 001-40657 | 10.9 | 03/10/2022 | |
| 10.12# | Amendment to Consulting Agreement by and between Richard A. Young and the Registrant, dated October 29, 2021. | 10-K | 001-40657 | 10.1 | 03/10/2022 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10.13 | Loan and Security Agreement between Pacific Western Bank (n/k/a PacWest Bancorp) and the Registrant, dated March 9, 2018, as amended on September 30, 2019, January 22, 2020 and December 30, 2020. | S-1/A | 333-257794 | 10.1 | 07/26/2021 | |
| 10.14 | Fourth Amendment to Loan and Security Agreement, dated December 20, 2021. | 8-K | 001-40657 | 10.1 | 12/21/2021 | |
| 10.15† | License Agreement between Flagship Pioneering Innovations V, Inc. and the Registrant, dated March 12, 2019. | S-1 | 333-257794 | 10.1 | 07/09/2021 | |
| 10.16† | Exclusive License Agreement between the Whitehead Institute for Biomedical Research and the Registrant, dated May 22, 2019. | S-1 | 333-257794 | 10.1 | 07/09/2021 | |
| 10.17† | Co-Exclusive License Agreement between the Whitehead Institute for Biomedical Research and the Registrant, dated May 22, 2019. | S-1 | 333-257794 | 10.1 | 07/09/2021 | |
| 10.18† | Development and Option Agreement between Acuitas Therapeutics, Inc. and the Registrant, dated October 5, 2020, as amended. | S-1 | 333-257794 | 10.2 | 07/09/2021 | |
| 10.19† | Non-Exclusive License Agreement between Acuitas Therapeutics, Inc. and the Registrant, dated March 22, 2021. | S-1 | 333-257794 | 10.2 | 07/09/2021 | |
| 10.20† | Collaboration and License Agreement between Nitto Denko Corporation and the Registrant, dated October 12, 2022. | | | | | * |
| 10.21 | Lease Agreement between BMR-325 Vassar Street LLC and the Registrant, dated November 30, 2017. | S-1/A | 333-257794 | 10.1 | 07/26/2021 | |
| 10.22 | Lease Agreement between Omega Therapeutics, Inc. and ARE-MA Region No, 94, LLC. | 10-K | 001-40657 | 10.1 | 03/10/2022 | |
| 10.23 | Amendment to Shared Space Agreement between Omega Therapeutics, Inc. and Senda Biosciences, Inc., dated January 31, 2022. | 10-K | 001-40657 | 10.1 | 03/10/2022 | |
| 21.1 | Subsidiaries of the Registrant. | 10-K | 001-40657 | 21.1 | 03/10/2022 | |
| 23.1 | Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm. | | | | | * |
| 31.1 | Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a). | | | | | * |
| 31.2 | Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a). | | | | | * |
| 32.1 | Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350. | | | | | ** |
| 32.2 | Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350. | | | | | ** |
| 101.INS | Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document. | | | | | * |

| | | |
|---|---|---|
| 101.SCH | Inline XBRL Taxonomy Extension Schema Document | * |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document | * |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document | * |
| 101.LAB | Inline XBRL Taxonomy Extension Label Linkbase Document | * |
| 101.PRE | Inline XBRL Taxonomy Extension Presentation Linkbase Document | * |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) | * |

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* Filed herewith.
** Furnished herewith.
# Indicates management contract or compensatory plan.
† Portions of this exhibit (indicated by asterisks) have been redacted in compliance with Regulation S-K Item 601(b)(10)(iv).

**Item 16. Form 10-K Summary**
None.

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Omega Therapeutics, Inc.

Date: March 1, 2023

By: /s/ Mahesh Karande

**Mahesh Karande**
**President and Chief Executive Officer**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

| Name | Title | Date |
|---|---|---|
| /s/ Mahesh Karande<br>**Mahesh Karande** | President, Chief Executive Officer and Director (principal executive officer) | March 1, 2023 |
| /s/ Joshua Reed<br>**Joshua Reed** | Chief Financial Officer (principal financial officer and principal accounting officer) | March 1, 2023 |
| /s/ Noubar B. Afeyan<br>**Noubar B. Afeyan, Ph.D.** | Chairman of the Board of Directors | March 1, 2023 |
| /s/ Rainer Boehm<br>**Rainer Boehm** | Director | March 1, 2023 |
| /s/ Luke M. Beshar<br>**Luke M. Beshar** | Director | March 1, 2023 |
| /s/ Elliott M. Levy<br>**Elliott M. Levy, M.D.** | Director | March 1, 2023 |
| /s/ John Mendlein<br>**John Mendlein, Ph.D., J.D.** | Director | March 1, 2023 |
| /s/ Mary T. Szela<br>**Mary T. Szela** | Director | March 1, 2023 |
| /s/ Richard A. Young<br>**Richard A. Young, Ph.D.** | Director | March 1, 2023 |

## INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of Omega Therapeutics, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Omega Therapeutics, Inc. and its subsidiary (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2022 and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

**Change in Accounting Principle**

As discussed in Note 2 to the financial statements, the Company adopted FASB Accounting Standards Codification Topic 842, Leases, and related amendments, on January 1, 2022, using the modified retrospective transition method.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ *Deloitte & Touche LLP*

Boston, Massachusetts

March 1, 2023

We have served as the Company's auditor since 2020.

**Omega Therapeutics, Inc.**
**Consolidated Balance Sheets**
**(in thousands, except share and per share amounts)**

| | December 31, 2022 | December 31, 2021 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 70,615 | $ 186,482 |
| Marketable securities | 54,063 | 38,845 |
| Accounts receivable, due from related party | 618 | 257 |
| Prepaid expenses and other current assets | 12,294 | 3,702 |
| Total current assets | 137,590 | 229,286 |
| Property and equipment, net | 4,195 | 3,605 |
| Operating lease right-of-use assets, net | 3,668 | — |
| Restricted cash | 341 | 341 |
| Other assets | 204 | 101 |
| Total assets | $ 145,998 | $ 233,333 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 3,107 | $ 2,109 |
| Accrued expenses | 13,841 | 9,475 |
| Other current liabilities | 159 | 399 |
| Lease liabilities, current | 1,524 | — |
| Long-term debt, current portion | 3,333 | — |
| Total current liabilities | 21,964 | 11,983 |
| Lease liabilities, non-current | 1,120 | — |
| Long-term debt, net | 16,603 | 19,869 |
| Other liabilities | 340 | 853 |
| Total liabilities | 40,027 | 32,705 |
| Commitments and contingencies (Note 9) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2022 and December 31, 2021; no shares issued and outstanding as of December 31, 2022 and December 31, 2021 | — | — |
| Common stock, $0.001 par value; 200,000,000 shares authorized as of December 31, 2022 and December 31, 2021; 48,072,517 and 47,793,469 issued and outstanding as of December 31, 2022 and December 31, 2021, respectively | 48 | 48 |
| Additional paid-in capital | 343,608 | 335,147 |
| Accumulated other comprehensive loss | (479) | (62) |
| Accumulated deficit | (237,206) | (134,505) |
| Total stockholders' equity | 105,971 | 200,628 |
| Total liabilities and stockholders' equity | $ 145,998 | $ 233,333 |

*The accompanying notes are an integral part of these consolidated financial statements.*

**Omega Therapeutics, Inc.**
**Consolidated Statements of Operations and Comprehensive Loss**
**(in thousands, except share and per share amounts)**

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Collaboration revenue from related party | $ 2,073 | $ 144 |
| Operating expenses: | | |
| Research and development | 79,996 | $ 47,865 |
| General and administrative | 21,821 | 16,603 |
| Related party expense, net | 3,022 | 1,708 |
| Total operating expenses | 104,839 | 66,176 |
| Loss from operations | (102,766) | (66,032) |
| Other income (expense), net: | | |
| Interest income (expense), net | 222 | (910) |
| Change in fair value of warrant liability | — | (1,310) |
| Other expense, net | (157) | (28) |
| Total other income (expense), net | 65 | (2,248) |
| Net loss | $ (102,701) | $ (68,280) |
| Net loss per common stock attributable to common stockholders, basic and diluted | $ (2.14) | $ (3.05) |
| Weighted-average common stock used in net loss per share attributable to common stockholders, basic and diluted | 47,880,819 | 22,404,058 |
| Comprehensive loss: | | |
| Net loss | $ (102,701) | $ (68,280) |
| Other comprehensive loss: | | |
| Unrealized loss on marketable securities | (417) | (62) |
| Comprehensive loss | $ (103,118) | $ (68,342) |

*The accompanying notes are an integral part of these consolidated financial statements.*

**Omega Therapeutics, Inc.**
**Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)**
**(in thousands, except share amounts)**

| | PREFERRED STOCK - SERIES A | | PREFERRED STOCK - SERIES B | | PREFERRED STOCK - SERIES C | | COMMON STOCK | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | SHARES | PAR VALUE | SHARES | PAR VALUE | SHARES | PAR VALUE | SHARES | PAR VALUE | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED OTHER COMPREHENSIVE LOSS | ACCUMULATED DEFICIT | TOTAL STOCKHOLDERS' EQUITY |
| **As of January 1, 2021** | 56,775,232 | $ 26,708 | 32,399,999 | $ 48,517 | — | $ — | 4,465,351 | $ 5 | $ 1,592 | $ — | $ (66,225) | $ (64,628) |
| Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $132 | — | — | — | — | 41,833,328 | 125,368 | — | — | — | — | — | — |
| Issuance of common stock from initial public offering, net of issuance costs of $13,005 | — | — | — | — | — | — | 8,300,976 | 8 | 128,104 | — | — | 128,112 |
| Conversion of redeemable convertible preferred stock to common stock upon closing of initial public offering | (56,775,232) | (26,708) | (32,399,999) | (48,517) | (41,833,328) | (125,368) | 34,678,733 | 35 | 200,559 | — | — | 200,594 |
| Conversion of preferred stock warrant to common stock warrant upon closing of initial public offering | — | — | — | — | — | — | — | — | 1,434 | — | — | 1,434 |
| Cashless exercise of warrants | — | — | — | — | — | — | 82,193 | — | | — | — | — |
| Issuance of common stock for options exercised | — | — | — | — | — | — | 266,216 | — | 274 | — | — | 274 |
| Other comprehensive loss | — | — | — | — | — | — | — | — | — | (62) | — | (62) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 3,184 | — | — | 3,184 |
| Net loss | — | — | — | — | — | — | — | — | — | — | (68,280) | (68,280) |
| **As of December 31, 2021** | — | $ — | — | $ — | — | $ — | 47,793,469 | $ 48 | $ 335,147 | $ (62) | $ (134,505) | $ 200,628 |
| Issuance of common stock for options exercised | — | — | — | — | — | — | 279,048 | — | 708 | — | — | 708 |
| Other comprehensive loss | | | | | | | — | — | — | (417) | — | (417) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 7,753 | — | — | 7,753 |
| Net loss | — | — | — | — | — | — | — | — | — | — | (102,701) | (102,701) |
| **As of December 31, 2022** | — | $ — | — | $ — | — | $ — | 48,072,517 | $ 48 | $ 343,608 | $ (479) | $ (237,206) | $ 105,971 |

*The accompanying notes are an integral part of these consolidated financial statements.*

**Omega Therapeutics, Inc.**
**Consolidated Statements of Cash Flows**
**(in thousands)**

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| **Operating activities** | | |
| Net loss | $ (102,701) | $ (68,280) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation | 1,564 | 1,387 |
| Amortization of debt issuance costs and debt discount | 67 | 93 |
| Amortization of operating lease right-of-use assets | 3,626 | — |
| Accretion of discounts on marketable securities | 1,045 | 25 |
| Change in fair value of warrant liability | — | 1,310 |
| Change in fair value of success fee obligation | 13 | 6 |
| Non-cash interest expense | — | 164 |
| Stock-based compensation expense | 7,753 | 3,184 |
| Deferred rent | — | (157) |
| Loss on disposal of equipment | — | (3) |
| Changes in operating assets and liabilities: | | |
| Accounts receivable due from related party | (362) | (257) |
| Prepaid expenses and other current assets | (8,592) | (2,646) |
| Other assets | (3,763) | 156 |
| Accounts payable | 985 | 1,040 |
| Accrued expenses and other current liabilities | 3,233 | 6,379 |
| Other liabilities | (1,383) | (10) |
| Net cash used in operating activities | (98,515) | (57,609) |
| **Investing activities** | | |
| Purchases of property and equipment | (1,380) | (1,467) |
| Purchases of marketable securities | (57,415) | (38,932) |
| Proceeds from maturities of marketable securities | 40,735 | — |
| Net cash used in investing activities | (18,060) | (40,399) |
| **Financing activities** | | |
| Proceeds from issuance of redeemable convertible preferred stock | — | 125,500 |
| Payments for preferred stock issuance costs | — | (132) |
| Proceeds from initial public offering of common stock, net of commissions and underwriting discounts | — | 131,238 |
| Payments for initial public offering costs | — | (3,126) |
| Payment of success fee | — | (200) |
| Proceeds from debt financing | — | 8,000 |
| Payments of financing fees | — | (15) |
| Proceeds from exercise of stock options | 708 | 274 |
| Net cash provided by financing activities | 708 | 261,539 |
| **Net change in cash, cash equivalents and restricted cash** | (115,867) | 163,531 |
| Cash, cash equivalents and restricted cash—beginning of period | 186,823 | 23,292 |
| Cash, cash equivalents and restricted cash—end of period | $ 70,956 | $ 186,823 |
| **Reconciliation of cash, cash equivalents and restricted cash** | | |
| Cash and cash equivalents | $ 70,615 | $ 186,482 |
| Restricted cash | 341 | 341 |
| Cash, cash equivalents and restricted cash | $ 70,956 | $ 186,823 |
| **Supplemental disclosures of cash flow information** | | |
| Cash paid for interest | $ 1,263 | $ 754 |
| **Supplemental disclosure of noncash investing and financing activities** | | |
| Conversion of preferred stock to common stock | $ — | $ 200,594 |
| Reclassification of warrants to additional paid-in capital | $ — | $ 1,434 |
| Purchase of property and equipment included in accounts payable and accrued expenses | $ 13 | $ 44 |
| Fair value attributed to success fee obligation | $ — | $ 105 |

*The accompanying notes are an integral part of these consolidated financial statements.*

## 1. Nature of the Business and Basis of Presentation

### *Organization*

Omega Therapeutics, Inc. (the "Company" or "Omega") is a clinical-stage biotechnology company pioneering a systematic approach to use mRNA therapeutics as programmable epigenetic medicines by leveraging its OMEGA platform. The OMEGA 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. The OMEGA platform enables control of fundamental epigenetic processes to correct the root cause of disease by restoring aberrant gene expression to a normal range without altering native nucleic acid sequences. The Company was incorporated in July 2016 ("inception") as a Delaware corporation and its offices are in Cambridge, Massachusetts.

### *Liquidity and going concern*

Since its inception, the Company has devoted substantially all of its resources to building its platform and advancing development of its portfolio of programs, establishing and protecting its intellectual property, conducting research and development activities, organizing and staffing the Company, business planning, raising capital and providing general and administrative support for these operations. The Company is subject to risks and uncertainties common to early clinical-stage companies in the biotechnology industry including, but not limited to, technical risks associated with the successful research, development and manufacturing of product candidates, risks related to clinical development of product candidates, developments by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Current and future programs will require significant research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

In August 2021, the Company completed its initial public offering ("IPO") pursuant to which it issued and sold 8,300,976 shares of its common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. The Company received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

The Company expects that its cash, cash equivalents and marketable securities of $124.7 million at December 31, 2022, together with the net proceeds from the registered direct offering completed on February 27, 2023, will enable it to fund its operating expenses and capital expenditure requirements into the second half of 2024. However, additional funding will be necessary to fund future preclinical and clinical activities and to develop new product candidates. The Company expects to finance its future cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources.

### *COVID-19-Related Significant Risks and Uncertainties*

With the global COVID-19 pandemic continuing, the Company is following, and plans to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures.

The extent to which the COVID-19 pandemic and variants of the virus impacts the Company's business, its corporate development objectives, results of operations and financial condition, and the fair value of and market for its common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements, and the effectiveness of actions taken globally to contain and treat the disease. Disruptions to the global economy, disruption of global healthcare systems, and other significant impacts of the COVID-19 pandemic could have a material adverse effect on the Company's business, financial condition, results of operations and growth prospects.

While the COVID-19 pandemic did not significantly impact the Company's business or results of operations during the year ended December 31, 2022, the length and extent of the pandemic, its consequences, and containment efforts will determine the future impact on the Company's operations and financial condition.

***Basis of Presentation***

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC"), and Accounting Standards Update ("ASU"), of the Financial Accounting Standards Board ("FASB"). All amounts herein are expressed in U.S. dollars ("USD") unless otherwise noted.

**2. Summary of significant accounting policies**

***Principles of consolidation***

The accompanying consolidated financial statements include the accounts of Omega Therapeutics, Inc. and its wholly owned subsidiary, Omega Therapeutics Security Corporation, which is a Massachusetts subsidiary. All intercompany transactions and balances have been eliminated in consolidation.

***Use of estimates***

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances.

Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the selection of useful lives of property and equipment, the fair values of certain financial instruments issued prior to the IPO (common stock, redeemable convertible preferred stock, and warrants), the fair value of the success fee obligation, the incremental borrowing rate used in the calculation of lease liabilities, research and development expenses, certain judgments regarding revenue recognition and stock-based compensation. Actual results could differ from these estimates. Changes in estimates are reflected in reported results in the period in which they become known.

***Cash and cash equivalents***

Cash includes cash in readily available checking accounts, and cash equivalents include money market accounts and all highly liquid investments with an original maturity of three months or less from the date of purchase. Cash and cash equivalents are recorded at cost, which approximates fair value.

***Marketable securities***

The Company's marketable securities as of December 31, 2022 consisted of corporate debt securities and are classified as available-for-sale and are reported at fair value. Unrealized gains and losses on available-for-sale debt securities are reported as a component of accumulated other comprehensive loss in stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included as a component in other expense, net.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a

period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the consolidated statements of operations and comprehensive loss.

***Restricted cash***

Restricted cash represents collateral provided for letters of credit issued as a security deposit in connection with the Company's office lease.

***Concentrations of credit risk***

Financial instruments that are potentially subject to significant concentration of credit risk consist primarily of cash, cash equivalents, and marketable securities. The Company attempts to minimize the risk related to marketable securities by working with highly rated financial institutions that invest in a broad and diverse range of financial instruments as defined the Company. The Company has established guidelines relative to credit ratings and maturities intended to safeguard principal balances and maintain liquidity. The Company maintains its funds in accordance with its investment policy, which defines allowable investments, specifies credit quality standards and is designed to limit credit exposure to any single issuer.

***Guarantees and indemnifications***

As permitted under Delaware law, the Company indemnifies its officers, directors, consultants, and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through December 31, 2022 and 2021, the Company had not experienced any losses related to these indemnification obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related liabilities were established.

***Property and equipment***

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset category as follows:

| Asset category | Estimated useful life |
|---|---|
| Computer equipment and software | 3 years |
| Laboratory equipment and office furniture | 5 years |
| Leasehold improvements | Shorter of useful life or remaining lease term |

Upon retirement or sale, the cost of assets disposed of, and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are charged to expense as incurred.

***Accrued research and development expenses***

The Company estimates accrued research and development expenses based on its estimates of the services received and efforts expended pursuant to quotes and contracts with third-party service providers, including contract research organizations ("CROs") and contract development and manufacturing organizations ("CDMOs") that supply, conduct and manage preclinical and clinical studies on the Company's behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to its vendors will exceed the level of services provided and result in a prepayment of the expense, in which it will be evaluated for current or long-term classification based on when it is expected to be realized. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts the accrual or the amount of prepaid expenses accordingly.

***Debt issuance costs***

Costs incurred in connection with the issuance of the Company's long-term debt have been recorded as a direct reduction against the debt and amortized over the life of the associated debt as a component of interest expense using the effective interest method.

***Warrant liability***

Warrants for the purchase of Series A redeemable convertible preferred stock ("Series A Preferred Stock") issued in connection with the loan and security agreement ("Loan Agreement"), as amended, with Pacific Western Bank ("PWB") were classified as a liability on the consolidated balance sheets at their fair value on the date of issuance. At the end of each reporting period, the change in estimated fair value during the period was recognized as a component of other expense, net in the consolidated statements of operations and comprehensive loss. The fair value of the warrants was remeasured at the end of each reporting period until the closing of the IPO, at which time the liabilities were reclassified to an equity component as the outstanding warrants automatically became warrants to purchase common stock.

***Success fee obligation***

The Loan Agreement, as amended, with PWB, requires the Company to pay a success fee ("success fee obligation") upon the occurrence of a specified liquidity event as described in the Loan Agreement, as amended. The Company determined that this obligation represented a freestanding derivative instrument. Accordingly, the success fee obligation was classified as a liability on the Company's consolidated balance sheets and initially recorded at fair value, with changes in fair value for each reporting period recognized in other expense, net in the consolidated statements of operations and comprehensive loss. The fair value of such obligation is remeasured at the end of each reporting period until the liability is settled.

***Deferred rent***

The Company's real estate operating leases provide for scheduled annual rent increases throughout the lease terms. The Company adopted ASU 2016-02, and related amendments, on January 1, 2022 using the modified retrospective transition method. Upon adoption the Company's operating lease right-of-use assets were adjusted for accumulated deferred rent, and no additional deferred rent was recorded during the year ended December 31, 2022.

For the year ended December 31, 2021, the Company recognized the effects of the scheduled rent increases on a straight-line basis over the full terms of the leases. Tenant improvement allowances, if any, provided by a landlord are recorded as deferred rent and amortized as reductions to rent expense over the lease terms.

***Equity issuance costs***

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity as a reduction of proceeds generated as a result of the offering. Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statement of operations. Upon closing of the IPO, deferred offering costs were derecognized and recorded against the IPO proceeds as a reduction to additional paid-in capital. There were no deferred offering costs as of December 31, 2022 and 2021.

***Impairment of long-lived assets***

The Company evaluates its long-lived assets, which consist primarily of property and equipment and operating lease right-of-use assets for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. There were no impairment losses recognized during the years ended December 31, 2022 and 2021.

***Fair value measurements***

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

***Redeemable convertible preferred stock***

The Company classified redeemable convertible preferred stock as temporary equity on the consolidated balance sheet because it could become redeemable upon occurrence of a deemed liquidation event that is outside of the Company's control. Upon completion of the Company's IPO, all of the Company's then outstanding redeemable convertible preferred stock was automatically converted into common stock.

***Revenue recognition***

Revenue recognized to-date is solely generated from the collaboration agreement with PM (CF) Explorations, Inc., or PMCo. The Company recognizes revenue in accordance with ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments, or, collectively, ASC 606.

At inception, the Company determines whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when performance obligation is satisfied. The Company only applies the five-step model to contracts when it determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, the Company applies judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in management's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction

price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer can use and benefit from the license. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

At the inception of each arrangement that includes milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's are not considered probable of being achieved and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. To date, the Company has not recognized any milestone revenue.

Deferred revenue arises from amounts received in advance of the culmination of the earnings process and is recognized as revenue in future periods as performance obligations are satisfied. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability.

***Research and development expenses***

Research and development expenses are charged to expense as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries and bonuses, stock-based compensation, employee benefits, facilities costs, laboratory supplies, depreciation, consulting fees, cost of licensing technology, milestone payment, and external contract research and development and manufacturing expenses. Costs for certain research and development activities are recognized based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

***Stock-based compensation***

The Company's stock-based compensation program allows for grants of incentive stock options, non-qualified stock options, stock appreciation rights, and restricted stock awards, restricted stock units and other stock-based awards to employees, directors and consultants.

The Company recognizes all stock-based compensation awards to employees and non-employees as expense in the consolidated statements of operations and comprehensive loss based on their fair values. For stock option awards,

the Company estimates the fair value using the Black-Scholes option pricing model. The fair value of the Company's common stock is used to determine the fair value of restricted stock awards.

Stock-based compensation awards are subject to service vesting conditions, and forfeitures are recorded as they occur. Compensation expense related to awards to employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. The Company applies ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07"), in which the measurement date for non-employee awards is determined as the date of grant, and stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate, and (iv) expected dividends. Due to the lack of a public market for the Company's common stock prior to the IPO and lack of sufficient company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees and non-employees, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the options due to its lack of sufficient historical data. The risk-free interest rate is based on U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

***Patent costs***

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred as patents have no future alternative use.

***Income taxes***

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's consolidated financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that these assets may not be realized. As of December 31, 2022 and 2021, the Company has recorded a full valuation allowance against its deferred tax assets. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

***Comprehensive loss***

Comprehensive loss is defined as the change in stockholders' equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss includes net loss as well as other changes in stockholders' equity which includes certain changes in equity that are excluded from net loss. The Company's only element of other comprehensive loss is unrealized gains and losses on its marketable securities.

***Net loss per share***

The Company follows the two-class method when computing net loss per share, as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be

allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common stock outstanding for the period. Diluted net loss attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common stock outstanding for the period, including potential dilutive common shares assuming the dilutive effect of common stock equivalents.

The Company's redeemable convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2022 and 2021.

***Segment and geographic information***

Operating segments are defined as components of an entity about which discrete information is available for evaluation by the chief operating decision maker, or CODM, or decision-making group, in deciding how to allocate resources and in assessing performance. The CODM is the Company's Chief Executive Officer. The CODM views its operations as and manages its business in one operating segment operating exclusively in the United States.

***Recently issued accounting pronouncements***

*Leases*

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight- line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases under ASC Topic 840: Leases ("Topic 840").

The Company adopted ASU 2016-02, and related amendments, on January 1, 2022 using the modified retrospective approach transition method. As such, the adoption of ASU 2016-02 did not change the classification of any of the existing leases as of the transition date, and the prior period results are not adjusted or restated and continue to be reported in accordance with Topic 840. The Company has elected a package of practical expedients, under which an entity need not reassess whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases, or initial direct costs for any existing leases. The Company also elected not to separate lease and non-lease components and not to recognize leases with an initial term of 12 months or less.

The Company has real estate leases for its corporate offices and lab space located in Cambridge, Massachusetts. It determines if an arrangement contains a lease at contract inception. Operating lease assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. Lease payments are typically fixed and escalate over time. Variable payments relate to the Company's usage or share of the lessor's operating costs associated with the underlying asset and are recognized as incurred. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that it will exercise that option. The Company uses its incremental borrowing rate to calculate the lease liability when the implicit rate is not readily determinable. Lease expense is recognized on a straight-line basis over the lease term.

Upon the adoption of this standard, the Company recorded operating lease right-of-use assets of $4.4 million and corresponding operating lease liabilities of $5.1 million as of January 1, 2022. The difference between the value of the right-of-use assets and lease liabilities is due to the reclassification of existing deferred rent and unamortized lease

incentives as of January 1, 2022. The adoption of this standard did not materially impact the consolidated statement of operations and comprehensive loss and statement of cash flows as of the adoption date and for the periods presented. Refer to Note 9, *Commitments and contingencies*, for further discussion.

**3. Marketable Securities**

The following table summarizes the Company's marketable securities (in thousands):

| | December 31, 2022 | | |
|---|---|---|---|
| | Amortized cost | Gross unrealized losses | Fair value |
| Corporate debt securities | $ 54,542 | $ (479) | $ 54,063 |

| | December 31, 2021 | | |
|---|---|---|---|
| | Amortized cost | Gross unrealized losses | Fair value |
| Corporate debt securities | $ 38,907 | $ (62) | $ 38,845 |

The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2022, the balance in accumulated other comprehensive loss was comprised solely of activity related to marketable securities. There were no realized gains or losses recognized on the sale or maturity of marketable securities for the year ended December 31, 2022 and, as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss during the year.

As of December 31, 2022, the Company did not intend to sell, and was more than likely not required to sell, the debt securities in a loss position before recovery of their amortized cost bases. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment at December 31, 2022.

**4. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consisted of the following (in thousands):

| | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Prepaid clinical expenses | $ 5,232 | $ — |
| Prepaid research and development | 2,072 | 534 |
| Prepaid rent | 1,857 | 825 |
| Other receivables | 1,180 | 264 |
| Prepaid insurance | 1,020 | 1,500 |
| Prepaid other | 776 | 436 |
| Prepaid software | 157 | 143 |
| Prepaid expenses and other current assets | $ 12,294 | $ 3,702 |

**5. Property and Equipment, Net**

Property and equipment, net consists of the following (in thousands):

| | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Lab equipment | $ 6,121 | $ 4,822 |
| Leasehold improvements | 1,378 | 1,378 |
| Furniture and fixtures | 1,093 | 1,073 |
| Construction in process | 827 | 54 |
| Computer equipment | 190 | 129 |
| Total property and equipment | 9,609 | 7,456 |
| Less accumulated depreciation | (5,414) | (3,851) |
| Property and equipment, net | $ 4,195 | $ 3,605 |

Depreciation expense for the years ended December 31, 2022 and 2021 was $1.6 million and $1.4 million, respectively.

**6. Accrued Expenses**

Accrued expenses consist of the following (in thousands):

| | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Employee related expenses | $ 4,368 | $ 2,545 |
| Manufacturing costs | 4,303 | — |
| Research costs | 3,876 | 5,640 |
| Professional and consulting fees | 743 | 759 |
| Other | 429 | 500 |
| Interest | 122 | 31 |
| Total | $ 13,841 | $ 9,475 |

**7. Term Loan**

On March 9, 2018 (“Closing Date”), the Company entered into the Loan Agreement with Pacific Western Bank (“PWB”) to initially borrow $8.0 million. In conjunction with the Loan Agreement, the Company issued a warrant to PWB to purchase up to 200,000 shares of Series A Preferred Stock at the strike price of $0.50 per share. The warrant was exercisable for a 10-year period.

On September 30, 2019, the Company entered into an amendment to the Loan Agreement (the “First Amendment”), in which PWB made an additional term loan to the Company in an aggregate principal amount of

$12.0 million. In conjunction with the First Amendment, the Company also issued a warrant to purchase 350,000 shares of Series A Preferred Stock, which effectively restated and replaced the original warrant agreement. The strike price of the amended warrant is $0.50 per share, and the term remains unchanged, expiring in March 2028. As the warrants issued were freestanding financial instruments that were exercisable for contingently redeemable shares, they were initially recorded at fair value on the date of issuance as a liability, with a corresponding discount recorded against the face value of the term loan. The discount was accreted against the face value of the term loan over its remaining term as additional interest expense. The change in estimated fair value of the warrants during the period was remeasured at each reporting date and recognized as a component of other expense, net in the consolidated statements of operations and comprehensive loss.

Upon the closing of the IPO, the Company's outstanding warrants to purchase Series A Preferred Stock automatically became warrants to purchase an aggregate of 92,647 shares of common stock. As a result, the fair value of the warrants was reclassified to additional paid-in capital. Additionally, the remaining unamortized debt discount of $0.1 million related to the warrants was written off during the three months ended September 30, 2021. In August 2021, the holders of such warrants completed a cashless exercise of the warrants, resulting in the Company's issuance of 82,193 shares of its common stock, whereby 10,454 shares of common stock were withheld by the Company to pay for the exercise price of the warrants.

On January 22, 2020, the Loan Agreement was further amended (the "Second Amendment") to extend the principal repayment start date. The Loan Agreement was further amended on December 30, 2020 (the "Third Amendment") to extend the principal repayment date. The maturity date of the term loan was extended to June 30, 2023, and it was to be repaid beginning on June 30, 2021 in twenty-four equal installments, including interest at a floating annual rate equal to the greater of (i) 0.75% above the prime rate then in effect and (ii) 6.00%, due monthly starting the first month after December 30, 2020. As a result of the closing of Series C redeemable convertible preferred stock ("Series C Preferred Stock") in March 2021, the Company satisfied the cash proceeds milestone as defined in the Third Amendment, in which the Company received gross cash proceeds of more than $50.0 million from the issuance of new preferred stock prior to June 30, 2021. Accordingly, the principal repayment date of the term loan was further extended to December 31, 2021 and the maturity date was extended to December 31, 2023. There are no other changes to the terms as a result of the achievement of the cash proceeds milestone. In connection with the Third Amendment, the Company incurred $15 thousand of debt issuance costs, which have been recorded as a direct reduction against the term loan and amortized over the life of the associated term loan as a component of interest expense using the effective interest method.

In accordance with the Third Amendment, the Company was required to pay a success fee of $0.2 million upon the occurrence of a specified liquidity event, including an IPO. The Company determined that this obligation represented a freestanding financial instrument, and accordingly, the success fee obligation was classified as a liability on the Company's consolidated balance sheet as of December 31, 2020 and initially recorded at fair value, with changes in fair value for each reporting period recognized in other expense, net in the consolidated statements of operations and comprehensive loss. The fair value of such obligation was remeasured at the end of each reporting period until the liability was settled, for which it was settled and paid in August 2021 upon the completion of the IPO.

On December 20, 2021, the Company entered into an amendment to the Loan Agreement (the "Fourth Amendment"), in which PWB made an additional term loan in an aggregate principal amount of $20.0 million. The proceeds of the term loan pursuant to the Fourth Amendment were first applied to the repayment in full of all outstanding principal and accrued interest on the then outstanding term loan of $12.0 million; the remaining cash proceeds of $8.0 million was used for general working capital and for capital expenditures purposes. The maturity date of the additional term loan will be on September 30, 2025, and it will be repaid beginning on September 30, 2023 in twenty-four equal monthly installments, including interest at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%, due monthly starting the first month after December 20, 2021. The Company incurred $15 thousand of debt issuance costs, which was recorded as a direct reduction against the additional term loan and amortized over the life of the associated term loan as a component of interest expense using the effective interest method. Pursuant to the Fourth Amendment, the Company is also required to pay a success fee, ranging from $0.1 million to $0.2 million depending on the timing in achieving a specified liquidity event. The Company determined that this obligation represented a freestanding financial instrument, and it was classified as a liability on the Company's consolidated balance sheet and initially recorded at fair value, with changes in fair value for each reporting period recognized in other expense, net in the consolidated statements of

operations and comprehensive loss. The fair value of such obligation is remeasured at the end of each reporting period until the liability is settled.

Borrowings under the Loan Agreement, as amended, are collateralized by substantially all of the Company's personal property, other than its intellectual property. There are no financial covenants associated with the Loan Agreement, as amended; however, the Company is subject to certain affirmative and negative covenants to which the Company will remain subject until maturity.

As of December 31, 2022, $3.3 million of the net carrying amount of the term loan was classified as short-term and $16.6 million was classified as long-term based on the repayment start date. The Company's outstanding term loan balance was comprised of the following (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Principal | $ 20,000 | $ 20,000 |
| Unamortized debt discount | (64) | (131) |
| Net carrying amount | $ 19,936 | $ 19,869 |

The Company determined that the expected life of the debt was equal to the term on the term loan. The effective interest rate on the liability component ranged from 5.53% to 8.18% for the period from the date of issuance through December 31, 2022. The following table sets forth total interest expense recognized related to the term loan (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Contractual interest expense | $ 1,229 | $ 740 |
| Amortization of debt issuance costs and debt discount | 67 | 258 |
| Total interest expense | $ 1,296 | $ 998 |

At December 31, 2022 and December 31, 2021, accrued interest on the term loan was $121 thousand and $31 thousand, respectively.

The Company is required to repay the following principal amounts in connection with its term loan (in thousands):

| | |
|---|---|
| 2023 | 3,333 |
| 2024 | 10,000 |
| 2025 | 6,667 |
| Total | $ 20,000 |

**8. Fair Value of Financial Instruments**

The fair value of the Company's cash and cash equivalents and restricted cash are measured through quoted market prices; the fair value of the Company's marketable securities is determined based on the pricing inputs other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date. Other current assets, accounts payable and accrued liabilities approximate their fair values as of December 31, 2022 and 2021, due to their short-term nature. The carrying value of the Company's debt approximates its fair value due to its variable interest rate, which approximates a market interest rate. The warrant liability and the success fee obligation associated with the Loan Agreement, as amended, contain unobservable inputs that reflect the Company's own assumptions in which there is little, if any, market activity at the measurement date, thus the Company's warrant liability and the success fee obligation are measured at their fair values on a recurring basis using unobservable inputs.

The fair value of the Company's financial instruments is summarized in the table below (in thousands):

| | December 31, 2022 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Financial Assets** | | | | |
| Money market funds | $ 25,776 | $ — | $ — | $ 25,776 |
| Corporate Debt Securities | — | 54,063 | — | 54,063 |
| Total | $ 25,776 | $ 54,063 | $ — | $ 79,839 |
| | | | | |
| **Financial Liabilities** | | | | |
| Success fee obligation | $ — | $ — | $ 118 | $ 118 |

| | December 31, 2021 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Financial Assets** | | | | |
| Money market funds | $ 110,864 | $ — | $ — | $ 110,864 |
| Marketable securities | — | 38,845 | — | 38,845 |
| Total | $ 110,864 | $ 38,845 | $ — | $ 149,709 |
| | | | | |
| **Financial Liabilities** | | | | |
| Success fee obligation | $ — | $ — | $ 105 | $ 105 |

In accordance with the Fourth Amendment of the Loan Agreement with PWB, the Company will be required to pay a success fee upon the achievement of a certain liquidity event; accordingly, the related obligation is recorded as current liabilities on the consolidated balance sheets as it is deemed more probable than not by the Company to be settled in less than one year. The fair value of the success fee obligation was determined using the probability-weighted expected return method. The key estimates and assumptions impacting the fair value included the probability of achieving a specified liquidity event, the expected timing of achieving a liquidity event and the discount rate. The fair value of the success fee obligation is remeasured at each reporting period, with changes in fair value recognized in the consolidated statements of operations and comprehensive loss, until such liability was settled.

The following reflects the significant quantitative inputs used to determine the valuation of the success fee obligations for the years ended December 31, 2022 and 2021:

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Discount rate | 8.0 % | 5.5 % |
| Expected timing of achieving liquidity events (years) | 0.3 - 1.3 | 0.6 - 1.8 |
| Probability of achieving liquidity events | 75% -25% | 10% -90% |

The following table provides a roll-forward of the fair values of the Company's success fee obligation for which fair value is determined by Level 3 inputs (in thousands):

| | Success fee obligation from the Fourth Amendment |
|---|---|
| Fair value at January 1, 2022 | $ 105 |
| Change in fair value | 13 |
| Fair value at December 31, 2022 | $ 118 |

**9. Commitments and contingencies**

***Leases***

The Company has the following operating leases for its corporate offices and lab space located in Cambridge, Massachusetts.

*325 Vassar Street*

In 2017, the Company entered a noncancelable operating lease agreement to lease its office space at 325 Vassar Street, Cambridge, Massachusetts, which will expire in September 2024. The Company is required to pay property taxes, insurance, and normal maintenance costs. The operating lease contains predetermined fixed escalations of minimum rentals during the lease term. During 2018, the Company received $1.1 million of landlord-funded leasehold improvements related to the leased office space. Upon adoption of ASU 2016-02 on January 1, 2022 the Company's operating lease right-of-use assets were adjusted for accumulated deferred rent, and no additional deferred rent was recorded during the year ended December 31, 2022. In 2019 and 2020, the Company entered into sublease agreements with two related parties to sublease this office and laboratory space. Refer to Note 16, *Related party transactions*, for further details.

*20 Acorn Park Drive*

On July 13, 2020, the Company entered into a Shared Space Arrangement ("the Arrangement") with Senda Biosciences, Inc. (“Senda”, also formerly known as Kintai Therapeutics, Inc.) to share one-third of Senda’s 69,867 square feet of leased space at 20 Acorn Park Drive, Cambridge, Massachusetts. Senda is a related party as it is an affiliate of Flagship Pioneering (“Flagship”). The Arrangement commenced on August 1, 2020, and was set to expire on July 31, 2022 with two options to extend the term of the Arrangement for a period of 24 months each. The operating lease contains predetermined fixed escalations of minimum rentals during the lease term, and the Company is required to pay property taxes, insurance, and normal maintenance costs. In January 2022, the Company entered into an amendment to the Arrangement with Senda to exercise the option to renew the lease term for another 12 months. The lease term now expires in July 2023. The Company also modified certain provisions related to the extension term. In connection with the modifications in the amendment, the Company made an upfront payment of $2.9 million, which will cover the rent payment for the extended lease term. Additionally, upon the expiration of the extended lease term, the Company will receive $0.7 million from Senda for all furniture, fixtures and equipment owned by the Company that will remain at the lease property.

*One Charles Park*

On November 4, 2021, the Company entered into a lease with ARE-MA Region No. 94, LLC to lease an aggregate of approximately 89,246 rentable square feet of office and laboratory space located at One Charles Park, Cambridge, Massachusetts, 02142. The term of the lease is estimated to begin in the second quarter of 2023 and ends fifteen years after lease commencement, subject to certain extension rights. The base rent for the leased space will be $115.00 per square foot, subject to an annual upward adjustment of 3% of the then current rental rate, starting on the first anniversary of the first payment of rent under the lease, and other potential adjustments based on the Company’s utilization of certain tenant improvement allowances. In accordance with the lease agreement, the Company paid $0.8 million upon the execution of the lease, which will offset the first month's rent. Since the lease has not yet commenced, no right-of-use assets or lease liabilities were recognized on the Company’s consolidated balance sheet as of December 31, 2022.

*Disclosures under Topic 842*

As of December 31, 2022, the right-of-use assets associated with the Company’s operating leases were $3.7 million, which were recorded separately on the Company’s consolidated balance sheet. The corresponding operating lease liabilities were $2.6 million as of December 31, 2022, of which $1.5 million were recorded in current liabilities and $1.1 million were recorded in long-term liabilities on the Company’s consolidated balance sheet.

The right-of-use assets represent the Company’s right to use an underlying asset during the lease term and the related lease liabilities represent the Company’s obligation to make lease payments arising from the lease. Both the right-of-use assets and the corresponding liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. As the Company’s leases do not provide an implicit rate, the Company estimated the incremental borrowing rate based on the interest rate from the amended Term Loan, which was fully collateralized.

The following table summarizes the components of lease expense for the year ended December 31, 2022 (in thousands).

| | Year Ended December 31, 2022 |
|---|---|
| Operating lease expense | $ 3,820 |
| Variable lease expense | 1,357 |
| Total lease expense | $ 5,177 |

The variable lease expenses generally include common area maintenance, utilities and property taxes. Of the total lease expense, $3.9 million was recorded within research and development expenses and $1.2 million was recorded within general and administrative expenses in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2022. There were no short-term lease costs incurred during the year ended December 31, 2022.

The weighted average remaining lease term and discount rate related to the Company's leases were as follows:

| | December 31, 2022 |
|---|---|
| Weighted average remaining lease term (years) | 1.8 |
| Weighted average discount rate | 5.5 % |

Supplemental cash flow information relating to the Company's leases for the year ended December 31, 2022 were as follows (in thousands):

| | December 31, 2022 |
|---|---|
| Cash paid for amounts included in the measurement of lease liabilities | $ 2,637 |
| Operating lease assets obtained in exchange for lease liabilities | $ 4,393 |

As of December 31, 2022, the estimated minimum lease payments for 325 Vassar and 20 Acorn Park for each of the years ending December 31 were as follows (in thousands):

| | |
|---|---|
| 2023 | $ 1,563 |
| 2024 | 1,205 |
| Total minimum lease payments | 2,768 |
| Less: Imputed interest | (124) |
| Present value of operating lease liabilities | $ 2,644 |

Estimated minimum lease payments for One Charles Park are not included in the table above, as the lease is estimated to begin in the second quarter of 2023. The estimated minimum lease payments for One Charles Park are $6.0 million, $10.5 million, $10.9 million, $11.3 million and $147.6 million for 2023, 2024, 2025, 2026 and thereafter, respectively. The Company intends to sublease a portion of this facility to supplement its growth plan.

*Disclosures related to periods prior to Topic 842*

As of December 31, 2021, the future minimum lease payments for the Company’s facility operating leases for each of the years ending December 31 were as follows (in thousands):

| | |
|---|---|
| 2022 | $ 3,013 |
| 2023 | 10,711 |
| 2024 | 11,766 |
| 2025 | 10,879 |
| 2026 | 11,205 |
| Thereafter | 148,290 |
| Total minimum lease payments | $ 195,864 |

**10. License Agreements**

***Flagship Pioneering Innovations V, Inc.***

In March 2019, the Company entered into an exclusive license agreement with Flagship Pioneering Innovations V, Inc., an affiliate of Flagship, under which the Company was granted an exclusive, worldwide, royalty-bearing, sublicensable, transferable license under specified patent rights to develop, manufacture and commercialize licensed products (the "Flagship License"). Under the terms of the Flagship License, the Company is obligated to pay low single digit percentage royalties on net sales of licensed products by the Company. Royalties shall be paid by the Company on a country-by-country basis until expiration or abandonment of the last valid patent claim covering such licensed product in such country. The Company is also obligated to reimburse Flagship for patent prosecution costs.

The royalty payment is contingent upon sales of licensed products under the Flagship License. As such, when such expense is considered probable and estimable at the commencement of sales, the Company will account for the royalty expense as cost of sales for the amount it is obligated.

***Whitehead Institute for Biomedical Research***

In May 2019, the Company entered into an exclusive license agreement with the Whitehead Institute for Biomedical Research ("WIBR"), an affiliate of one of the Company's board members, under which the Company was granted an exclusive, worldwide, royalty-bearing, sublicensable license under specified patent rights to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes (the "WIBR Exclusive License"). Under the terms of the WIBR Exclusive License, the Company paid a nonrefundable upfront fee of less than $0.1 million upon the commencement of the exclusive license agreement. The Company is obligated to pay WIBR annual license maintenance fees of less than $0.1 million and low single digit percentage royalties on net sales of licensed products by the Company and its affiliates and sublicensees. Additionally, the Company is required to make milestone payments of up to $1.7 million in the aggregate for each of the first three licensed products (excluding backup products) upon the achievement of specified clinical and regulatory milestones. In addition, the Company is required to pay to WIBR a percentage of the non-royalty payments that it receives from sublicensees of the WIBR Exclusive License. This percentage ranges from zero to low double-digits and will be based upon the stage of development of the licensed product at the time such sublicense is executed.

In May 2019, the Company also entered into a co-exclusive license agreement with WIBR under which the Company was granted a co-exclusive, worldwide, royalty-bearing, sublicensable license under specified patent rights to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes (the "WIBR Co-Exclusive License"). Under the terms of the WIBR Co-Exclusive License, the Company paid a nonrefundable upfront fee of less than $0.1 million upon the commencement of the co-exclusive license agreement. The Company is obligated to pay WIBR annual license maintenance fees of less than $0.1 million and sub single digit percentage royalties on net sales of licensed products by the Company and its affiliates and sublicensees as well as low single digit percentage royalties on licensed service income received by the Company and its affiliates. Additionally, the Company is required to make milestone payments of up to $1.9 million in the aggregate for each of the first three licensed products (excluding backup products) upon the achievement of specified clinical and regulatory milestones. In addition, the Company is required to pay to WIBR annual fees of less than $0.1 million for each sublicense agreement.

For both of the years ended December 31, 2022 and 2021, the Company recognized expenses of less than $0.2 million for license maintenance fees and milestone payments. There was no outstanding payment due to WIBR as of December 31, 2022 and an immaterial amount outstanding as of December 31, 2021.

The annual maintenance fees will be recorded as an expense on an annual basis based on the stated amount for the applicable year. Upon determination that a milestone payment is probable to occur, the amount due will be recorded as research and development expense. Lastly, the royalty payments and the sublicense non-royalty payments are contingent upon sales of licensed products or execution of a sublicense agreement under the WIBR Exclusive and Co-Exclusive Licenses. As such, when such expenses are considered probable and estimable at the commencement of sales or execution of a sublicense agreement, the Company will accrue royalty expense and sublicense non-royalty payments, as applicable, for the amount the Company is obligated.

***Acuitas Therapeutics, Inc.***

In October 2020, the Company entered into a development and option agreement (the “Development and Option Agreement”) with Acuitas Therapeutics, Inc. (“Acuitas”). Under the terms of the Development and Option Agreement, the parties agreed to jointly develop certain products combining the Company’s gene modulating therapeutics with Acuitas' lipid nanoparticles. Additionally, in accordance with the Development and Option Agreement, the Company has options to obtain non-exclusive, worldwide, sublicensable licenses under Acuitas’ patents and know-how related to lipid nanoparticle technology (“Acuitas LNP Technology”) with respect to two specified targets (e.g., OEC constructs) (“Reserved Targets”) to develop and commercialize one or more therapeutic products relating to such targets. For each option and Reserved Target, the Company is obligated to pay an annual technology access fee and target reservation and maintenance fees collectively in the low-mid six figures until such Reserved Target is removed from the Reserved Target list or until the Company exercises an option with respect to such Reserved Target. In the event that the Company exercises the options, the Company will pay $1.5 million for the first non-exclusive license and $1.75 million for the second non-exclusive license. Under the terms of the Development and Option Agreement, the Company is also responsible for the full-time equivalent ("FTE") funding obligations, which is expected to be approximately $0.4 million per year, and reimbursements to Acuitas for certain development and material costs incurred by them.

In March 2021, the Company exercised the first option under the Development and Option Agreement and entered into a non-exclusive license agreement with Acuitas (the “Acuitas License Agreement”) under which the Company was granted a non-exclusive, worldwide, sublicensable license under the Acuitas LNP Technology to research, develop, manufacture, and commercially exploit products consisting of the Company’s gene modulating therapeutics and Acuitas’ lipid nanoparticles. In connection with the option exercise, the Company incurred an expense for the option exercise fee of $1.5 million. Under the Acuitas License Agreement, the Company is required to pay Acuitas an annual license maintenance fee in the high six figures until the Company achieves a certain development milestone. Acuitas is entitled to receive potential clinical and regulatory milestone payments of up to $18.0 million in the aggregate. With respect to the sale of each licensed products, the Company is also obligated to pay Acuitas low single digit percentage royalties on net sales of the licensed products by the Company and its affiliates and sublicensees in a given country until the last to occur, in such country, of (i) the expiration or abandonment of all licensed patent rights covering the licensed product, (ii) expiration of any regulatory exclusivity for the licensed product, or (iii) ten years from the first commercial sale of the licensed product.

During the years ended December 31, 2022 and 2021, the Company recorded an aggregate of $1.9 million and $3.3 million of research and development expenses, respectively, consisting of technology access fees, target reservation and maintenance fees, the costs of services performed by Acuitas, material costs and reimbursable costs.

The option exercise fee under the Development and Option Agreement was recorded as research and development expense upon the Company’s exercise of the first option. Additionally, the technology access fees, target reservation and maintenance fees, expenses associated with the FTE funding obligations and reimbursements for development and material costs incurred by Acuitas are recorded as research and development expense when incurred. The annual maintenance fee will be recorded as an expense on an annual basis based on the stated amount for the applicable year. Upon determination that a milestone payment is probable to occur, the amount due will be recorded as research and development expense. For the year ended December 31, 2022, $0.8 million has been recorded as research and development expense for these milestones. There were no milestones triggered, and no expense was recorded related to them for the year ended December 31, 2021. Lastly, the royalty payment is contingent upon sales of licensed products under the Acuitas License Agreement. As such, when such expenses are considered probable and estimable at the commencement of sales, the Company will accrue royalty expense for the amount the Company is obligated.

***Nitto Denko Corporation***

On October 12, 2022, the Company entered into a Collaboration and License Agreement (the "Nitto Agreement”) with Nitto Denko Corporation (“Nitto”), pursuant to which, among other things, Nitto granted the Company an exclusive, worldwide, royalty-bearing, fully transferable and fully sublicensable license under all intellectual property owned or controlled by Nitto relating to its lipid nanoparticle delivery technology.

Under the terms of the Nitto Agreement, the Company has made an upfront cash payment of $1.0 million, and developmental milestone payments of $1.0 million to Nitto in 2022. Both payments have been recorded as research and development expenses. The Company is also required to make up to $83.0 million in future payments to Nitto based upon the achievement of specified development, regulatory and sales milestones. The Company is also obligated to pay to Nitto tiered, single-digit percentage royalties on a country-by-country basis based on net sales of the licensed product, subject to reduction in specified circumstances. As such, when these expenses are considered probable and estimable, the Company will accrue expense for the amount the Company is obligated.

**11. Collaboration Agreements**

In November 2021, the Company entered into a five-year collaboration agreement with PMCo, an affiliate of Flagship, under which PMCo was granted an exclusive license covering specified patent rights of the Company's lipid nanoparticle technology to develop one or more therapeutic products to treat diseases related to the cystic fibrosis transmembrane conductance regulator gene, like cystic fibrosis. Under the terms of the agreement, the Company will perform certain research activities in accordance with the research plan, and PMCo will be solely responsible for, at its sole cost and expense, and will have sole discretion with respect to, developing, manufacturing, seeking regulatory approval for and commercializing licensed products. The Company expects to receive approximately $3.1 million in cost reimbursement through 2023 to fund the related research and development activities. The research plan funding may be adjusted upon mutual written agreement from both parties. Additionally, in the event PMCo is acquired or sold, the Company is entitled to receive a portion of the proceeds of such transaction, subject to various reductions and other amounts payable in accordance with the agreement.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, PMCo, is a customer. The Company determined that the research activities and the exclusive license granted under the collaboration agreement is considered as a single performance obligation, and therefore, the transaction price was allocated entirely to the single performance obligation. The Company recognizes revenue related to the single performance obligation over time as the underlying services are performed and/or external costs are incurred.

The total transaction price at December 31, 2022 was determined to be $5.4 million based on the current estimated required efforts to fulfill the performance obligation. This total includes an increase of $1.9 million resulting from an amendment agreed upon with PMCo in 2022. As of December 31, 2022, the remaining transaction price was estimated to be $3.1 million, which is expected to be recognized as revenue through 2023.

The Company recognized funded research and collaboration revenue of $2.1 million and $0.1 million in the consolidated statements of operations and comprehensive loss during the years ended December 31, 2022 and 2021, respectively. Additionally, the Company recognized less than $0.1 million of current deferred revenue as of December 31, 2022 based on the period the services are expected to be performed and/or related costs to be incurred. Costs incurred associated with this collaboration agreement were recorded as research and development expenses.

Pursuant to the agreement, we are entitled to receive a portion of the sales proceeds in the event PMCo is acquired or sold. At the end of each reporting period, the Company evaluates the probability of occurrence of such transaction. As of December 31, 2022, the Company determined that the proceeds from such transaction was not probable of recognition.

***Nitto Denko Corporation***

On October 12, 2022, the Company entered into a Collaboration and License Agreement with Nitto, pursuant to which, among other things, Nitto granted the Company an exclusive, worldwide, royalty-bearing, fully transferable and fully sublicensable license under all intellectual property owned or controlled by Nitto relating to its lipid nanoparticle delivery technology. See further discussion in Note 10, *License Agreements*.

**12. Preferred and Common Stock**

The Company's board of directors and stockholders approved an amendment to the Company's certificate of incorporation, which became effective on July 23, 2021. The amendment, among other things, effected a 1-for-3.777776 reverse stock split of the Company's issued and outstanding common stock, a proportional adjustment to the conversion price for Series A, B and C Preferred Stock and to the exercise prices and number of shares of common stock underlying the outstanding stock options. All share, per share and additional paid in capital amounts for all periods presented in the accompanying financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect the reverse stock split.

In August 2021, the Company completed its IPO pursuant to which it issued and sold 8,300,976 shares of its common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. The Company received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

In connection with the completion of the IPO, the Company's board of directors and stockholders approved the Company's Amended and Restated Certificate of Incorporation to, among other things, provide for 200,000,000 authorized shares of common stock with a par value of $0.001 per share and 10,000,000 authorized shares of preferred stock with a par value of $0.001 per share.

The holders of common stock are entitled to one vote for each share of common stock. Subject to the payment in full of all preferential dividends to which the holders of the preferred stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of any voluntary or involuntary liquidation, dissolution, or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

As of December 31, 2022, the Company has reserved an aggregate of 8,438,573 shares of common stock for the potential exercise of outstanding stock options under its equity incentive plans. Upon the effectiveness of the 2021 Incentive Award Plan ("2021 Plan"), the Company ceased granting awards under the 2017 Equity Incentive Plan ("2017 Plan"), and the 4,069,183 shares of common stock subject to outstanding stock options issued under the 2017 Plan may become available for future issuance under the 2021 Plan to the extent such stock options are forfeited.

**13. Equity Incentive Plan**

**2017 Equity Incentive Plan**

In June 2017, the Company's board of directors adopted the 2017 Plan, which provided for the grant of qualified incentive stock options and nonqualified stock options, restricted stock or other awards to the Company's employees and non-employees for the issuance or purchase of shares of the Company's common stock. As of December 31, 2022, there were no shares available for future grants under the 2017 Plan and a total of 4,069,183 shares of the Company's common stock were subject to outstanding stock options issued under the 2017 Plan.

The 2017 Plan is administered by the Company's board of directors or a committee thereof to the extent the Company's board of directors has delegated its power or authority under the 2017 Plan. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the common stock on the date of grant. Stock options awarded under the 2017 Plan expire 10 years after the grant date unless the board of directors sets a shorter term. Incentive stock options and nonqualified stock options granted to employees and non-employees typically vest over four years. Certain stock options provide for accelerated vesting if there is a change in control, as defined in the 2017 Plan.

***2021 Incentive Award Plan***

The Company's board of directors adopted, and the Company's stockholders approved, the 2021 Plan in July 2021. The 2021 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards, and subsequent to

the IPO, all equity-based awards are granted under the 2021 Plan. The Company initially reserved 2,960,000 shares of its common stock for future issuance under the 2021 Plan, and such number of shares of common stock is subject to an annual increase on the first day of each calendar year, beginning on January 1, 2022 and ending on and including January 1, 2031, equal to the lesser of (i) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by the board of directors. As of December 31, 2022, there were 1,152,352 shares available for future grants under the 2021 Plan, and a total of 4,369,390 shares of the Company's common stock were subject to outstanding stock options issued under the 2021 Plan.

The Company recorded stock-based compensation expense as research and development and general and administrative expenses in the consolidated statements of operations and comprehensive loss as follows (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Research and development | $ 4,026 | $ 1,205 |
| General and administrative | 3,727 | 1,979 |
| Total stock-based compensation expense | $ 7,753 | $ 3,184 |

***Stock Options***

The assumptions used in the Black-Scholes option-pricing model for stock options granted were as follows:

| | Year ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Expected volatility% | 76.09% - 77.62% | 76.73% - 80.18% |
| Weighted-average risk-free interest rate% | 2.69 % | 1.12 % |
| Expected dividend yield% | 0.00 % | 0.00 % |
| Weighted-average expected term (in years) | 6.11 | 6.09 |

A summary of option activity under the Company's equity incentive plans during the year ended December 31, 2022 was as follows:

| | Number of options | Weighted average exercise price | Weighted average remaining contractual life (years) | Aggregate intrinsic value [1] (in thousands) |
|---|---|---|---|---|
| Outstanding as of January 1, 2022 | 5,476,484 | $ 4.90 | 8.64 | $ 39,325 |
| Granted | 3,992,386 | 7.45 | | |
| Exercised | (279,048) | 2.54 | | |
| Forfeited | (658,352) | 6.79 | | |
| Expired | (92,897) | 8.41 | | |
| Outstanding as of December 31, 2022 | 8,438,573 | 6.00 | 8.40 | 12,976 |
| Vested and expected to vest as of December 31, 2022 | 8,438,573 | 6.00 | 8.40 | 12,976 |
| Exercisable as of December 31, 2022 | 2,742,075 | $ 3.53 | 7.26 | $ 8,480 |

[1] The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options that were in the money as of December 31, 2022.

The weighted-average grant date fair value per share of stock options granted during the years ended December 31, 2022 and 2021 was $5.08 and $5.71, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2022 and 2021 was $1.0 million and $1.8 million, respectively.

As of December 31, 2022, there was $24.2 million of unrecognized compensation cost related to unvested stock options, which is expected to be recognized over a weighted-average period of approximately 2.6 years.

**14. Net Loss per Share Attributable to Common Stockholders**

For periods in which the Company reports a net loss attributable to common stockholders, potentially dilutive securities have been excluded from the computation of diluted net loss per share as their effects would be anti-dilutive. Therefore, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands except share and per share amounts):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Numerator: | | |
| Net loss attributable to common stockholders | $ (102,701) | $ (68,280) |
| Denominator: | | |
| Weighted average number of common stock, basic and diluted | 47,880,819 | 22,404,058 |
| Net loss per common stock attributable to common stockholders, basic and diluted | $ (2.14) | $ (3.05) |

The Company excluded the following potential common stock, presented based on amounts outstanding at period end, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

| | As of December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Outstanding options to purchase common stock | 8,438,573 | 5,476,484 |

**15. Income taxes**

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

| | Year ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| U.S. federal statutory income tax rate | 21.0% | 21.0% |
| State income taxes, net of federal benefit | 7.1 | 7.6 |
| Research and development tax credits | 4.3 | 3.0 |
| Non-deductible / non-taxable permanent items | (0.5) | (0.9) |
| Change in valuation allowance | (32.0) | (30.8) |
| Other | 0.1 | 0.1 |
| Effective income tax rate | 0.0% | 0.0% |

The components of the Company's deferred taxes are as follows (in thousands):

| | Year ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 40,157 | $ 34,194 |
| Research and development credit carryforwards | 11,013 | 5,638 |
| Accrued expenses | 1,098 | 879 |
| Stock-based compensation | 1,726 | 528 |
| Intangible assets | 136 | 152 |
| IRC 174 R&D capitalization | 20,024 | — |
| Lease liabilities | 722 | — |
| Unrealized gain/loss | 325 | — |
| Total deferred tax assets | 75,201 | 41,391 |
| Less: valuation allowance | (74,005) | (41,203) |
| Deferred tax assets, net | 1,196 | 188 |
| Deferred tax liabilities: | | |
| Depreciation | (194) | (182) |
| Operating lease right-of-use assets | (1,002) | — |
| Unrealized gain/loss | — | (6) |
| Total deferred tax liabilities | (1,196) | (188) |
| Net deferred taxes | $ — | $ — |

The Company had no income tax expense due to the operating loss incurred for the years ended December 31, 2022 and 2021. Management has evaluated the positive and negative evidence bearing upon the realizability of the Company's net deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefits of the net deferred tax assets. As a result, the Company has recorded a full valuation allowance as of December 31, 2022 and 2021. The valuation allowance increased by $32.8 million in 2022, due to the increase in deferred tax assets, primarily resulting from the net operating loss carryforwards, research and development tax credits, IRC 174 R&D Capitalization, stock-based compensation expense and deductible accrued expenses.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the Internal Revenue Code, certain substantial changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards, which could be used annually to offset future taxable income. The Company has not completed a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the Company's formation due to the significant complexity and cost associated with such study and because there could be additional changes in control in the future. As a result, the Company is not able to estimate the effect of the change in control, if any, on the Company's ability to utilize net operating loss and research and development credit carryforwards in the future.

As of December 31, 2022, the Company had $147.8 million of federal and $143.9 million of state net operating loss carryforwards. If not utilized, both the federal and state net operating loss carryforwards have components that begin to expire starting in 2036. Of the $147.8 million federal net operating loss carryforwards, $142.3 million of net operating loss generated from 2018 to 2022 will not expire. Additionally, as of December 31, 2022, the Company had $7.8 million of federal and $4.0 million of Massachusetts tax credits that expire starting in 2036 and 2031, respectively.

As of December 31, 2021, the Company had $125.8 million of federal and $123.0 million of state net operating loss carryforwards. If not utilized, both the federal and state net operating loss carryforwards have components that begin to expire starting in 2036. Of the $125.8 million federal net operating loss carryforwards, $120.3 million of net operating loss generated from 2018 to 2021 will not expire. Additionally, as of December 31, 2021, the Company had $3.4 million of federal and $2.8 million of Massachusetts tax credits that expire starting in 2036 and 2031, respectively.

As of December 31, 2022 and 2021, the Company had no uncertain tax positions. The Company will recognize both interest and penalties associated with unrecognized tax benefits as a component of income tax expense. The Company has not recorded any interest or penalties for unrecognized tax benefits since its inception.

The Company filed income tax returns in the United States and the Commonwealth of Massachusetts in all tax years since inception. All tax years remain open to examination by these jurisdictions, as carryforward attributes generated in past years may be adjusted in a future period. The Company is not currently under examination by the Internal Revenue Service or any other taxing authority for these years.

**16. Related Party Transactions**

The majority ownership of the Company is held by Flagship, in which it holds shares representing approximately 54% of the Company's outstanding voting stock as of December 31, 2022. Flagship historically provided management services to the Company, and we reimburse Flagship for certain expenses, including insurance and benefits, and related fees, and software licenses incurred on the Company's behalf. For the years ended December 31, 2022 and 2021, the Company incurred $1.7 million and $1.0 million, respectively, primarily for reimbursable expenses. These expenses are recorded as related party expense in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2022 and December 31, 2021, there was an immaterial amount of outstanding payments due to Flagship.

In September 2020, the Company sublet the entire space of its 325 Vassar Street facility, approximately 19,404 square feet, to LARONDE, Inc. ("LARONDE", formerly known as VL50, Inc.), which is an affiliate of Flagship. The sublease term will expire at the end of the Company's lease agreement with the landlord in September 2024. The rental rate for the sublease arrangement is equal to the Company's rental obligation per the agreement with BMR-325 Vassar Street LLC, reduced by the sublease income received from Cygnal Therapeutics, Inc. ("Cygnal"), approximating $1.3 million per year. The sublessee is obligated to pay all real estate taxes and costs related to the subleased premises, including cost of operations, maintenance, repair, replacement and property management. Under the sublease agreement, the Company received rental income, which was recorded as a reduction of rental expense, of $2.3 million and $2.0 million during the years ended December 31, 2022 and 2021, respectively. Such rental income was reflected as a reduction of related party expense in the accompanying consolidated statements of operations and comprehensive loss. There was no outstanding receivable due from LARONDE as of December 31, 2022 and December 31, 2021.

In September 2019, the Company sublet approximately 1,445 square feet of its 325 Vassar Street facility to Cygnal, which is an affiliate of Flagship, for two years. The lease term was to continue on a month-to-month basis until advanced notice is provided to the Company. Cygnal gave notice, terminated the agreement and vacated the property in May 2022. The rental rate for the sublease arrangement was equal to the Company's rental obligation per the agreement with BMR-325 Vassar Street LLC, approximating $0.1 million per year. The sublessee was obligated to pay all real estate taxes and costs related to the subleased premises, including cost of operations, maintenance, repair, replacement and property management. Under the sublease agreement, the Company received rental income of less than $0.1 million for each of the years ended December 31, 2022 and 2021, which was recorded as a reduction of rental expenses. Such rental income was reflected as a reduction of related party expense in the accompanying consolidated statements of operations and comprehensive loss. There was no outstanding receivable due from Cygnal as of December 31, 2022 and December 31, 2021.

Refer to other related party transactions as described in Note 9, *Commitments and contingencies*, Note 10, *License agreements* and Note 11, *Collaboration agreement*.

**17. Employee benefits**

In 2018, the Company established a defined-contribution plan under Section 401(k) of the Internal Revenue Code, or the 401(k) Plan. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. On May 1, 2022, the Company began matching 50% of employee contributions of up to 6% of eligible compensation contributed on a pre-tax and/or Roth after-tax basis to the 401(k) Plan. During the year ended December 31, 2022, the Company made matching contributions totaling $0.5 million. The Company made no contributions to the 401(k) Plan during the year ended December 31, 2021.

**18. Subsequent Events**

On February 27, 2023, the Company completed a registered direct offering of common stock pursuant to which it issued and sold 6,920,415 shares of its common stock at a purchase price of $5.78 per share and secured approximately $39.7 million in net proceeds after deducting estimated offering expenses. As part of this registered direct offering, Flagship acquired 3,323,310 shares of common stock.

Certain information marked as [***] has been excluded from this exhibit because it is both (i) not material and (ii) the type that the Registrant treats as private or confidential.

**COLLABORATION AND LICENSE AGREEMENT BY AND BETWEEN**
**NITTO DENKO CORPORATION AND**
**OMEGA THERAPEUTICS, INC.**

**Dated as of October 12, 2022**

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**LIST OF APPENDICES**

# COLLABORATION AND LICENSE AGREEMENT

**THIS COLLABORATION AND LICENSE AGREEMENT** (this "**Agreement**"), dated as of October 12, 2022 (the "**Effective Date**"), is made by and between Nitto Denko Corporation, located at Grand Front Osaka, 4-20 Ofuka-cho, 33rd Floor, Kita-ku, Osaka, Japan ("**Nitto**"), on the one hand, and Omega Therapeutics, Inc., located at 20 Acorn Park Drive, Cambridge, MA 02140 ("**Omega**"), on the other hand. Omega and Nitto are referred to herein individually as a "**Party**" and collectively as the "**Parties**".

**WHEREAS**, Nitto develops lipid nanoparticles ("**LNP**") through the use of its proprietary delivery system to deliver oligonucleotides such as mRNA constructs to target cells and has rights to certain Intellectual Property (as defined below) related thereto;

**WHEREAS**, Omega has developed certain Epigenomic Controllers (as defined below);

**WHEREAS**, Omega and Nitto and its Affiliate (as defined below), Nitto BioPharma, Inc., located at 10618 Science Center Drive, San Diego, CA 92121 ("**NBPI**") entered into the Memorandum of Understanding, dated September 8, 2021 (the "**Original MOU**"), and subsequently entered into a Master Development Agreement, dated as of December 16, 2021 (the "**MDA**"), to evaluate the potential feasibility of the efficacy of combining Omega's proprietary Epigenomic Controllers with Nitto's LNP delivery technology for development of LNP formulations of such Epigenomic Controllers in lung and two (2) other organs to be agreed upon by the Parties, in order to determine Omega's interest in obtaining a separate, exclusive license (a "**License**") to the such LNP delivery system and related Intellectual Property with respect to each Collaboration Target (as defined below) under terms described in Appendix B to the MDA;

**WHEREAS**, under the MDA, a Feasibility Study (as defined in the MDA) has been ongoing with respect to MYC in lung as the 1st Collaboration Target (as defined in Appendix B of the MDA);

**WHEREAS** pursuant to Section 3.4(b) of the MDA, Nitto granted Omega an exclusive option to be granted an exclusive license under Nitto's Intellectual Property, to research, develop, make, have made, use, offer for sale, sell, have sold and import LNPs consisting of Epigenomic Controllers; and

**WHEREAS**, on June 13, 2022 (the "**MOU Effective Date**"), Omega and Nitto and NBPI executed a Memorandum of Understanding ("**MOU**"), pursuant to which, among other thing, Omega exercised its option with respect to the Collaboration Target and paid a portion of the upfront fee agreed upon, Nitto granted Omega an exclusive license with respect to the Licensed Product (as defined below), and the Parties agreed to binding terms set forth in a term sheet attached as Appendix A thereto, and agreed to negotiate a definitive agreement to supersede the MDA with respect to the Collaboration Target and the MOU;

**NOW, THEREFORE**, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the amount and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

## ARTICLE 1
## Definitions

The following terms and their correlatives will have the following meanings:

1.1 "**Affiliate**" of a Person or entity means any other Person which (directly or indirectly) is controlled by, controls or is under common control with such Person. For the purposes of this definition, the term "**control**" (including, with correlative meanings, the terms "**controlled by**" and "**under common**

**control with**") as used with respect to an entity will mean (a) in the case of a corporate entity, direct or indirect ownership of voting securities entitled to cast more than fifty percent (50%) of the votes in the election of directors, or (b) in the case of a non-corporate entity, direct or indirect ownership of more than fifty percent (50%) of the equity interests with the power to direct the management and policies of such entity; *provided that* if local Law restricts foreign ownership, control will be established by direct or indirect ownership of the maximum ownership percentage that may, under such local Law, be owned by foreign interests.

1.2 "**Budget**" has the meaning set forth in Section 3.3(b)(ii).

1.3 "**Business Day**" means mean a day on which banking institutions in Boston, Massachusetts, USA, San Diego, California and Osaka, Japan are open for business.

1.4 "**Calendar Quarter**" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; *provided*, that (a) the first Calendar Quarter of the Term will begin on the MOU Effective Date and end on the first to occur of March 31, June 30, September 30 or December 31 thereafter and the last Calendar Quarter of the Term will end on the last day of the Term, and (b) the first Calendar Quarter of a Royalty Term for a Licensed Product in a country will begin on the First Commercial Sale of such Licensed Product in such country and end on the first to occur of March 31, June 30, September 30 or December 31 thereafter and the last Calendar Quarter of a Royalty Term will end on the last day of such Royalty Term.

1.5 "**Calendar Year**" means the period beginning on the MOU Effective Date and ending on December 31 of the first calendar year in which the MOU Effective Date falls, and thereafter each successive period of twelve (12) consecutive calendar months beginning on January 1 and ending on December 31; *provided*, that the final Calendar Year shall end on the last day of the Term on a country-by- country and Licensed Product-by-Licensed Product basis.

1.6 "**cGMP**" means current Good Manufacturing Practices as specified in Parts 210 and 211 of Title 21 of the U.S. C.F.R., ICH Guideline Q7A, or equivalent Laws of an applicable Regulatory Authority at the time of manufacture.

1.7 "**Change of Control**" means any of the following: (a) the sale or disposition of all or substantially all of the assets of a Party or its direct or indirect controlling Affiliate to a Third Party, other than to an entity of which more than fifty percent (50%) of the voting capital stock are owned after such sale or disposition by shareholders of such Party or its direct or indirect controlling Affiliate (in either case, whether directly or indirectly through any parent entity); or (b) (i) the acquisition by a Third Party, alone or together with any of its Affiliates, other than an employee benefit plan (or related trust) sponsored or maintained by such Party or any of its Affiliates, of more than fifty percent (50%) of the outstanding shares of voting capital stock of such Party or its direct or indirect controlling Affiliate, or (ii) the acquisition, merger or consolidation of such Party or its direct or indirect controlling Affiliate with or into another Person or entity, other than, in the case of this clause (b), an acquisition or a merger or consolidation of such Party or its controlling Affiliate in which the holders of shares of voting capital stock of such Party or its controlling Affiliate, as the case may be, immediately prior to such acquisition, merger or consolidation will beneficially own, directly or indirectly, at least fifty percent (50%) of the shares of voting capital stock of the acquiring Third Party or the surviving corporation in such acquisition, merger or consolidation, as the case may be, immediately after such acquisition, merger or consolidation.

1.8 "**CMO**" has the meaning set forth in Section 2.4.

1.9 "**Collaboration Target**" means MYC in lung, which for clarity is the 1st Collaboration Target (as defined in Appendix B of the MDA). This Agreement does not cover any other Collaboration Target (as defined in Appendix B of the MDA).

1.10 "**Combination Product**" means a product that includes at least one additional active ingredient other than the Epigenomic Controller in the Licensed Product sold in conjunction with or used in combination with a Licensed Product (whether packaged together or packaged separately but sold together for a single price).

1.11 "**Commercialize**" or "**Commercialization**" means, together with all correlative meanings, the import, export, marketing, promotion, sale or distribution of a product, including commercial activities conducted in preparation for a product launch.

1.12 "**Competitive Infringement**" has the meaning set forth in Section 7.1.

1.13 "**Competing Product**" means any product comprised of or incorporating Epigenomic Controller(s) that are the same as the Epigenomic Controller(s) in the Licensed Product.

1.14 "**Confidential Information**" has the meaning set forth in Section 8.1.

1.15 "**Control**" or "**Controlled**" means, with respect to any Intellectual Property, a Party owns or has a license to use and practice such and has the right to grant a license or sublicense to such Intellectual Property without violating the terms of any agreement with any Third Party

1.16 "**Covered**" and "**Covering**" means, with reference to a Licensed Product, that without the licenses granted to Omega hereunder, the manufacture, Development or Commercialization of such Licensed Product would infringe a Valid Claim.

1.17 "**Debar**", "**Debarred**" or "**Debarment**" means (a) being debarred, or being subject to a pending debarment, pursuant to section 306 of the FDCA, 21 U.S.C. § 335a, (b) being listed by any federal and/or state agencies, excluded, debarred, suspended or otherwise made ineligible to participate in federal or state healthcare programs or federal procurement or non-procurement programs (as that term is defined in 42 U.S.C. § 1320a-7b(f)), or being subject to any pending process by which any such listing, exclusion, debarment, suspension or other ineligibility could occur, (c) being disqualified by any government or regulatory agency, or being subject to a pending disqualification proceeding, or (d) being convicted of a criminal offense related to the provision of healthcare items or services or being subject to any pending criminal action related to the provision of healthcare items or services.

1.18 "**Develop**", "**Developed**" or "**Development**" means, together with all correlative meanings, pre-clinical and clinical drug development activities, conducted before or after obtaining Marketing Authorization Approval that are reasonably related to or leading to the development, preparation, and submission of data and information to a Regulatory Authority for the purpose of obtaining, supporting or expanding Marketing Authorization Approval or to the appropriate body for obtaining, supporting or expanding pricing and reimbursement approval, including without limitation, all activities related to preclinical testing, assay development and validation, *in vivo* testing, biomarker development and validation, toxicology, pharmacokinetic profiling, design and conduct of clinical trials and any other clinical trials or studies, regulatory affairs, statistical analysis, report writing, and regulatory material creation and submission (including the services of outside advisors and consultants in connection therewith).

1.19 "**Development Milestone Events**" has the meaning set forth in Section 4.2.

1.20 "**Development Milestone Payments**" has the meaning set forth in Section 4.2.

1.21 "**Disclosing Party**" has the meaning set forth in Section 8.1.

1.22 "**Dollars**" means United States dollars.

1.23 "**Efficacy Endpoint**" is defined in Section 1.82.

1.24 "**Effective Date**" has the meaning set forth in the Preamble.

1.25 "**EMA**" means the European Medicines Agency, or any successor, that coordinates the scientific review of human pharmaceutical products under the centralized licensing procedures of the European Union.

1.26 "**Epigenomic Controller**" means any agent, including, but not limited to, a polypeptide, a peptide, a nucleic acid (*e.g.*, RNA or DNA, including both modified and unmodified forms of RNA and DNA), a nucleic acid-encoded polypeptide, a gene expression modifying molecule, an epigenetic editing molecule, and a non-biologic organic molecule (*i.e.* a "small molecule"), that, in each case, directly or indirectly regulates expression of one or more Genes via epigenetic modification of an Insulated Genomic Domain that includes the Gene(s), an enhancer sequence, a promoter sequence, a coding sequence, a non- coding sequence, a CTCF-binding site, a cis regulatory element sequence, or any combination of the aforementioned elements.

1.27 "**Executive Officers**" means in the case of Nitto, the chief of the nucleic acid medicine business division, and in the case of Omega, Omega's Chief Executive Officer.

1.28 "**FDA**" means the United States Food and Drug Administration, and any successor agency with similar responsibilities.

1.29 "**First Commercial Sale**" means the first sale for use or consumption for which revenue has been recognized of any Licensed Product in a country after all required Marketing Authorization Approvals for commercial sale of such Licensed Product have been obtained in such country; *provided, however*, that the following shall not constitute a First Commercial Sale: (a) any sale between Omega, Affiliate or Sublicensee or between the Parties (or their respective Affiliates or sublicensees); (b) any use of such Licensed Product in clinical trials or non-clinical development activities with respect to the Licensed Product by or on behalf of Omega, or disposal or transfer of such Licensed Product for a bona fide charitable purpose; (c) compassionate use; (d) early access programs also known as named patients programs and temporary authorization for use for the administration of the Licensed Product to named individuals who do not meet the clinical trial enrolment or after the completion of a clinical trial.

1.30 "**FTE**" means the work of a full-time person for one year, or more than one person working the equivalent of a full-time person for one year, where "full-time" is determined by the standard practices in the biopharmaceutical industry in the geographic area in which such personnel are working; *provided, however*, that for purposes of performance of the agreed activities for the Technology Transfer, including scientific management oversight as reasonably required, means 1840 hours per year.

1.31 "**FTE Costs**" mean the US$200/hr, such FTE Costs representing reimbursement for all costs of FTEs in providing such activities (including salaries, benefits, and overhead.).

1.32 "**GAAP**" means generally accepted accounting principles in the United States.

1.33 "**Gene**" means (a) a naturally occurring human gene, including, but not limited to, all coding, non-coding and regulatory regions thereof, as identified by the applicable transcript identifier (i.e. NCBI Refseq transcript ID), gene identifier (i.e. NCBI Refseq Gene ID), gene name and synonyms and nucleotide sequence coordinates, gene transcript and nucleotide sequence; (b) any naturally occurring, non- coding region of the human genome including, but not limited to, transcriptional regulatory elements, non-protein coding RNA and intergenic regions; (c) a gene encoded by any nucleotide sequence of a human pathogen residing in a human cell in vivo; or (d) any gene that is not already covered by subclause (a) or
(b) above, together with any variants of such gene, including, but not limited to, the wild type and naturally occurring mutant and allelic variants, provided however that any such variant (i) encodes a protein with substantially similar mechanism of action and biological activity to the protein product of the original (reference) gene and (ii) has a coding region with eighty-five percent (85%) sequence identity to the coding region of the original (reference) gene.

1.34 "**IND**" means an application submitted to a Regulatory Authority to initiate human clinical trials, including (a) an Investigational New Drug application or any successor application or procedure filed with the FDA, (b) any equivalent of a U.S. Investigational New Drug application in any country outside the United States, and (c) all supplements and amendments that may be filed with respect to the applications described in clause (a) or (b) above of this Section 1.34.

1.35 "**Indemnification Claim Notice**" has the meaning set forth in Section 9.6(c).

1.36 "**Indemnified Party**" has the meaning set forth in Section 9.6(c).

1.37 "**Indemnifying Party**" has the meaning set forth in Section 9.6(c).

1.38 "**Initial Payment Date**" has the meaning set forth in Section 4.1.

1.39 "**Insolvency Legislation**" has the meaning set forth in Section 10.4.

1.40 "**Insulated Genomic Domain**" means a continuous segment of a chromosome that (a) is bounded on both ends by a CTCF-binding site, and (b) contains one or more Genes whose expression is regulated by chromosomal elements that lie between the CTCF-binding sites and is insulated from regulation by chromosomal elements that lie beyond the CTCF-binding site boundaries on the chromosome.

1.41 "**Intellectual Property**" means all inventions, discoveries, technical information, know- how, data, results, technology, trade secrets, processes, methods, ideas, physical, chemical or biological materials, whether or not patentable, and any patents, trademarks, service marks, registered designs, copyrights, database rights, and design rights and applications for any of the above.

1.42 "**Joint Development Plan**" is defined in Section 3.1(a).

1.43 "**Joint IP**" means any Project IP that constitute an improvement, enhancement or derivative of both the Nitto Background Technology and the Omega Background Technology, whether patentable or not. Joint IP includes combinations of (a) both Nitto Material and Omega Material, or (b) improvements, enhancements or derivatives of both Omega Material and Nitto Material. Joint IP does not include Nitto IP or Omega IP.

1.44 "**Joint Patents**" means Patents that Cover Joint IP.

1.45 "**Joint Steering Committee**" or "**JSC**" has the meaning set forth in Section 3.3(a).

1.46 "**Know-How**" means all Nitto Materials and all confidential and proprietary commercial, technical, scientific and other know-how and information, trade secrets, knowledge, technology, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, specifications, data and results (including biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, preclinical, clinical, safety, manufacturing and quality control data and know-how, and including study designs and protocols), in all cases, *provided that* such information is confidential and proprietary, and regardless of whether patentable, in written, electronic or any other form now known or hereafter developed.

1.47 "**Late-Stage Development**" means, with respect to a product, that in which first dosing under Phase 2 Studies has been initiated.

1.48 "**Law**" or "**Laws**" means all laws, statutes, rules, regulations, orders, judgments or ordinances having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision.

1.49 "**License Agreement**" has the meaning set forth in the Preamble.

1.50 "**Licensed Field**" means all human therapeutic, palliative and/or prophylactic uses and applications.

1.51 "**Licensed IP**" means (a) all Intellectual Property, including the Patents listed in Appendix A, and other Nitto Background Technology, that is necessary or useful to research, Develop, make, have made, use, sell, have sold, offer for sale, or import a Licensed Product in the Licensed Field in the Licensed Territory, (b) Nitto IP, and (c) Nitto's interest in Joint IP. For the avoidance of doubt, "useful" Intellectual Property means Intellectual Property that is not strictly necessary but helpful for Omega to research, Develop, make, have made, use, sell, have sold, offer for sale, or import a Licensed Product in the Licensed Field in the Licensed Territory. "Useful" Intellectual Property includes but not limited to the Intellectual Property that makes formulation of loaded LNP more efficient, cheaper, and cleaner.

1.52 "**Licensed Product**" means any product directed to the Collaboration Target that
(a) consists of (i) one LNP composition, which is approved by the JSC (the "**Nominated LNP**"), and (ii) contains one or more Epigenomic Controllers Controlled by Omega (the "**OEC**") and (b) (i) but for the licenses granted to Omega by Nitto, would infringe at least one Valid Claim in the Licensed IP, or (ii) incorporates or otherwise makes use of the data, results or Know-How included in the Licensed IP. For the avoidance of doubt, only one specific formulation of a Nominated LNP and an OEC as determined by JSC will be a Licensed Product at any given time; provided that the JSC has the authority to change or replace the Nominated LNP or OEC in such formulation.

1.53 "**Licensed Territory**" means worldwide.

1.54 "**LNP**" has the meaning set forth in the first recital.

1.55 "**Losses**" has the meaning set forth in Section 9.6(a).

1.56 "**Major Market Country**" means the United States, Japan, the United Kingdom, Germany, France, Spain, Italy or the People's Republic of China.

1.57 "**Marketing Authorization Approval**" or "**MAA**" means, with respect to a country or extra-national territory, any and all approvals (including a New Drug Application or Biologics License Application approved by the FDA), licenses, registrations or authorizations of any Regulatory Authority

necessary in order to commercially distribute, sell or market a product in such country or some or all of such extra-national territory.

1.58 "**MDA**" has the meaning set forth in the third recital.

1.59 "**Milestone Event**" means Development Milestone Events and Sales Milestone Events.

1.60 "**Milestone Payments**" means Development Milestone Payments and Sales Milestone Payments.

1.61 "**Modified Material**" means the material created by Nitto after the date of the Original MOU (including under the Joint Development Plan) and that is combination of a specific Omega Material with the specific Nitto Material utilizing, respectively the Omega Background Technology and the Nitto Background Technology.

1.62 "**MOU**" has the meaning set forth in the sixth recital.

1.63 "**MOU Effective Date**" has the meaning set forth in the sixth recital.

1.64 "**mRNA Construct**" means any mRNA that encodes one or more Protein Targets and any associated non-coding sequences, including any cap sequence, 5'UTR, 3'UTR, and any polyadenylation sequences. The term "**mRNA Construct**" also includes the chemistry of natural and non-natural nucleic acids, and other chemical modifications associated with such mRNA and associated non-coding sequences.

1.65 "**Net Sales**" means, with respect to the Licensed Product, the gross amount earned and realized or recognized as revenue in accordance with GAAP by Omega and its Affiliates or Sublicensees for sales or other dispositions of such Licensed Product to a Third Party (other than Sublicensees for resale, but including distributors for resale), less (solely to the extent included in such gross amount):

(a) [***];

(b) [***];

(c) [***];

(d) [***];

(e) [***];

(f) [***]; and

(g) [***].

Net Sales will not include any payments among Omega, its Affiliates and Sublicensees. Net Sales shall not be imputed to transfers of Licensed Products for use in clinical trials, non-clinical development activities or other development activities with respect to Licensed Products by or on behalf of the Parties, for bona fide charitable purposes, named patient or early access programs, or for compassionate use or for Licensed Product samples, if no monetary consideration is received for such transfers.

Such amounts will be determined from the books and records of Omega and its Affiliates and Sublicensees, maintained in accordance with GAAP consistently applied.

Net Sales for any Combination Product will be calculated on a country-by-country basis by multiplying actual Net Sales of such Combination Product by the fraction A/(A+B), where A is the average price paid for the Licensed Product contained in such Combination Product sold separately in finished form in such country, and B is the average invoice price paid for the other active ingredients contained in such Combination Product sold separately in finished form in such country, if such Licensed Product and such other active ingredients are each sold separately in such country.

Net Sales of the Licensed Product for any Combination Product if the Licensed Product or other active ingredients in such Combination Product are not sold separately in such country, will be calculated by multiplying the Net Sales of the Combination Product by a fraction, the numerator of which will be the fair market value of the Licensed Product as if sold separately, and the denominator of which will be the aggregate fair market value of all the other active ingredients of such Combination Product, including the Licensed Product, as if sold separately. In such event, Omega will in good faith make a determination of the respective fair market values of each component included in the Combination Product and will notify Nitto of such determination and provide Nitto with Omega's basis for such determination. If Nitto in good faith does not agree with such determination, then the fair market value of each component of a Combination Product will be a determined by a Third Party expert selected by Omega and reasonably acceptable to Nitto.

1.66 "**Nitto Background Technology**" means Intellectual Property relating to the Nitto Material that (a) is Controlled by Nitto or its Affiliates and (b) exists as of and/or was conceived prior to the effective date of the Original MOU, or is Developed or obtained by Nitto or its Affiliates independently of the Original MOU, the MDA, the MOU and this Agreement without the use of Omega's Confidential Information or the Omega Material. For purposes of clarity, Nitto Background Technology includes the Nitto Material, but does not include Modified Material.

1.67 "**Nitto Indemnitees**" has the meaning set forth in Section 9.6(a).

1.68 "**Nitto IP**" means, regardless of inventorship, Project IP that is solely an improvement, enhancement or derivative of Nitto Background Technology and that is not an improvement, enhancement or derivative of the Omega Background Technology. For the avoidance of doubt, Nitto IP expressly includes combinations of (a) nucleic acids that are not limited to Omega Material or an improvement, enhancement or derivative of Omega Material, and (b) Nitto Material or an improvement, enhancement or derivative of Nitto Material. Nitto IP does not include Joint IP or Omega IP.

1.69 "**Nitto Material**" means LNPs used to deliver oligonucleotides, such as mRNA constructs to target cells Controlled by Nitto or its Affiliates, excluding Modified Material.

1.70 "**Nitto Patents**" means all Patents Covering Nitto IP.

1.71 "**Omega Background Technology**" means Intellectual Property relating to the Omega Material that (a) is Controlled by Omega or its Affiliates and (b) exists as of and/or was conceived prior to the effective date of the Original MOU, or is Developed or obtained by Omega or its Affiliates independently of the Original MOU, the MDA, the MOU and this Agreement without the use of Nitto's Confidential Information or the Nitto Material. For purposes of clarity, Omega Background Technology includes the Omega Material, but does not include Modified Material.

1.72 "**Omega Indemnitees**" has the meaning set forth in Section 9.6(b).

1.73 "**Omega IP**" means regardless of inventorship, the Project IP that is solely an improvement, enhancement or derivative of any Omega Background Technology and that is not an improvement, enhancement or derivative of Nitto Background Technology. For the avoidance of doubt, Omega IP expressly includes combinations of (a) Omega Material or an improvement, enhancement or derivative of Omega Material, and (b) LNPs that are not limited to Nitto Material or an improvement, enhancement or derivative of Nitto Material. Omega IP does not include Joint IP or Nitto IP.

1.74 "**Omega Material**" means Epigenomic Controllers Controlled by Omega or its Affiliates, excluding Modified Material.

1.75 "**Omega Patents**" means all Patents that Cover Omega IP.

1.76 "**Orange Book**" means FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*.

1.77 "**Party**" and "**Parties**" has the meaning set forth in the Preamble.

1.78 "**Patent(s)**" means an (a) issued patent, a patent application, and a future patent issued from any such patent application, (b) a future patent issued from a patent application filed in any country worldwide that claims priority from a patent or patent application included in (a), (c) any additions, divisions, continuations, continuations-in-part, invention certificates, substitutions, reissues, reexaminations, extensions, registrations, utility models, supplementary protection certificates and renewals based on any patent or patent application under (a) or (b), but not including any rights that give rise to regulatory exclusivity periods (other than supplementary protection certificates, which will be treated as "**Patents**" hereunder), and (d) any counterpart of any patent or patent application under (a), (b) or (c) filed in any country worldwide.

1.79 "**Patent Costs**" means the reasonable, documented, out-of-pocket costs and expenses paid to outside legal counsel, and filing and maintenance expenses, actually and reasonably incurred by a Party in prosecuting and maintaining Patents.

1.80 "**Person**" means any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

1.81 "**Phase 1 Study**" means a human clinical trial of the Licensed Product in any country, the primary purpose of which is the determination of safety and which may include the determination of

metabolism and pharmacologic actions of the Licensed Product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness, as more fully defined in 21 C.F.R.
§ 312.21(a) or its successor regulation, or the equivalent in a country other than the United States.

1.82 "**Phase 1/2 Study**" means a human clinical trial (or any arm thereof) of a pharmaceutical or biologic product with the endpoint of (a) determining initial tolerance, safety, metabolism, pharmacokinetic or pharmacodynamic information in single dose, single ascending dose, multiple dose, or multiple ascending dose regimens, and (b) evaluating its effectiveness for a particular indication or indications in one or more specified doses or its short term tolerance and safety, as well as its pharmacokinetic and pharmacodynamic information in patients with the indications under study, that is prospectively designed to generate sufficient data (if successful) to commence a Phase 3 Study for such product (the endpoint in this Section 1.82(b) being referred to as the "**Efficacy Endpoint**"), and that satisfies the requirements of U.S. federal regulation 21 C.F.R. §§ 312.21(a) and (b) and its successor regulation or equivalents in other jurisdictions.

1.83 "**Phase 2 Study**" means a human clinical trial of the Licensed Product in any country, the primary purpose of which is to evaluate the effectiveness of the Licensed Product for a particular indication or indications in patients with the disease or condition under study and to determine the common short- term side effects and risks associated with the Licensed Product, as more fully defined in 21 C.F.R.
§ 312.21(b) or its successor regulation, or the equivalent in a country other than the United States.

1.84 "**Phase 3 Study**" means a human clinical trial of the Licensed Product in any country, the primary purpose of which is to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the Licensed Product and to provide an adequate basis for physician labeling, as more fully defined in 21 C.F.R. § 312.21(c) or its successor regulation, or the equivalent in a country other than the United States.

1.85 "**PMDA**" means the Japan Pharmaceuticals and Medical Devices Agency, and any successor agency with similar responsibilities.

1.86 "**Project IP**" means Intellectual Property (but excluding the Study Data) that is discovered, generated, made or reduced to practice in the performance of this Agreement or the MDA with respect to the Collaboration Target and the Joint Development Plan. For clarity, Project IP can be either Joint IP, Nitto IP or Omega IP.

1.87 **"Purple Book**" means FDA's *List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations.*

1.88 "**Receiving Party**" has the meaning set forth in Section 8.1."**Regulatory Authority**" means each federal, national, multinational, state, provincial or local regulatory agency, department, bureau or other governmental authority with authority over the testing, manufacture, use, storage, import, promotion, marketing or sale of, or the granting of Marketing Authorization Approval for, the Licensed Product in a country or territory including (a) the FDA, (b) the EMA, and (c) the PMDA.

1.89 "**R&D Term**" means the term beginning on the MOU Effective Date, and ending upon the first submission of an IND with respect to the Licensed Product.

1.90 "**Regulatory Exclusivity**" means with respect to any country or other jurisdiction in the Territory, an additional market protection, other than Patent protection, granted by a Regulatory Authority in such country or other jurisdiction which confers an exclusive commercialization period during which Omega or its Affiliates or Sublicensees have the exclusive right to market and sell the Licensed Product in

such country or other jurisdiction through data exclusivity, market exclusivity, or supplemental protection certificates, if any, covering the Licensed Product in the applicable country.

1.91 "**Royalty**" has the meaning set forth in Section 4.4(a).

1.92 "**Royalty Term**" has the meaning set forth in Section 4.4(c).

1.93 **"Sales Milestone Events**" has the meaning set forth in Section 4.3.

1.94 **"Sales Milestone Payments**" has the meaning set forth in Section 4.3.

1.95 "**Specified IP**" means the Patents listed in Appendix D and patents and patent applications, filed in the United States or any other country or jurisdiction, that claim priority to a patent application or priority patent application listed in Appendix D, their respective additions, divisions, continuations, continuations-in-part, invention certificates, substitutions, reissues, reexaminations, extensions, registrations, utility models, supplementary protection certificates, renewals, and the counterparts and equivalents thereof.

1.96 "**Study Data**" means any data and data analyses that are generated in the performance of a Work Plan (as defined in the MDA) related to the Collaboration Target, and pursuant to the Joint Development Plan.

1.97 "**Sublicensee**" means any Third Party that is granted a sublicense as permitted by Section 2.3, either directly by Omega or its Affiliates or indirectly by any other Sublicensee hereunder.

1.98 "**Technology Transfer**" has the meaning set forth in Section 2.4.

1.99 "**Technology Transfer Plan**" has the meaning set forth in Section 2.4.

1.100 "**Term**" has the meaning set forth in Section 10.1.

1.101 "**Third Party**" means any Person other than Omega, Nitto and their respective Affiliates.

1.102 "**Third Party Claims**" has the meaning set forth in Section 9.6(a).

1.103 "**Valid Claim**" means a claim of (a) an issued and unexpired patent included in the Licensed IP which has not been abandoned and which has not been disclaimed, canceled, revoked or held invalid or unenforceable by a court or administrative agency of competent jurisdiction from which no further appeal is possible and that is not admitted to be invalid or unenforceable through reissue, re- examination, disclaimer or otherwise, or (b) a pending patent application included in the Licensed IP which claim is being actively prosecuted and which has not been (i) canceled, (ii) withdrawn from consideration,
(iii) finally determined to be unallowable by the applicable governmental authority (and from which no appeal is or can be taken), (iv) abandoned, or (v) pending for more than [***] from the earliest priority date of such patent application.

## ARTICLE 2
## License Grant; Technology Transfer

2.1 License by Nitto. Nitto hereby grants to Omega a royalty-bearing, exclusive, fully transferable, and fully sublicensable (through multiple tiers) license under the Licensed IP to research,

Develop, Commercialize, make, have made, use, sell, have sold, offer for sale, import the Licensed Product in the Licensed Field throughout the Licensed Territory during the Term.

2.2 License Limitations. No licenses or other rights are granted by Nitto hereunder to use any trademark, trade name, trade dress or service mark owned or otherwise Controlled by Nitto or any of its Affiliates. All licenses and other rights are or will be granted only as expressly provided in this Agreement, and no other licenses or other rights are or will be created or granted by either Party hereunder by implication, estoppel or otherwise.

2.3 Sublicensing Rights.

(a) Transfer. The license granted in Section 2.1 is transferable only upon a permitted assignment of this Agreement in accordance with Section 11.11.

(b) Omega Sublicenses. The license granted in Section 2.1 may be sublicensed (with the right to sublicense through multiple tiers), in full or in part, by Omega, its Affiliates or its Sublicensees to Omega's Affiliates and Third Parties, *provided*, that for any sublicense to Third Parties:

(i) Omega shall obtain Nitto's prior consent for a sublicense to a direct competitor of Nitto listed in Appendix B, which will be fully reviewed by Nitto annually, with any updates to be mutually agreed by the Parties;

(ii) Each sublicense will be in writing and on terms consistent with and subject to the terms of this Agreement;

(iii) Omega will provide Nitto with a copy of any sublicense agreement with a Sublicensee for Commercialization rights within thirty (30) days of execution thereof, which sublicense agreement may be redacted as necessary to protect commercially sensitive information and will be treated as Omega's Confidential Information hereunder;

(iv) Omega will be responsible and liable for any and all obligations of such Sublicensee as if such Sublicensee were Omega hereunder; and

(v) Any sublicense granted by Omega to any rights licensed to it hereunder will terminate immediately upon the termination of the license from Nitto to Omega and its Affiliates with respect to such rights; *provided*, that such sublicensed rights will not terminate if, as of the effective date of such termination by Nitto pursuant to Sections 10.2 or 10.4, a Sublicensee is not in material default of its obligations under its sublicense agreement, and within ninety (90) days of such termination, the Sublicensee agrees in writing to be bound directly to Nitto under a license agreement substantially equivalent to this Agreement with respect to Omega's rights and obligations hereunder, substituting such Sublicensee for Omega; provided, however, that Nitto will not be required to enter into any such license agreement with any Person that could reasonably be expected to harm Nitto's reputation.

(c) Subcontractors. For clarity purposes, Omega is entitled to engage contract research organizations, contract manufacturing organizations and other service providers for the Development and manufacture of the Licensed Product on behalf of Omega, including under the Joint Development Plan as provided in Section 3.1(c). To the extent such contract organizations and service providers require a license to perform such subcontracted activities under applicable Laws, Omega is entitled to grant a research or manufacturing sublicense (as applicable).

2.4 Technology Transfer. Within thirty (30) days of the Effective Date the Parties shall discuss in good faith and agree upon a preliminary plan (the "**Technology Transfer Plan**") for Nitto to transfer the formulation process, raw materials supply chain and analytical methods for the manufacture of the Licensed Product and related Know-How, to Omega or any cGMP contract manufacturing organizations ("**CMO**") designated and notified to Nitto in advance by Omega (the "**Technology Transfer**"). The Parties will mutually agree in good faith upon any revisions to the Technology Transfer Plan.

2.5 Exclusivity. During the Term, neither Nitto nor any of its Affiliates will, directly or indirectly, except as otherwise permitted in this Agreement, either alone or with or for any Third Party, Develop, manufacture or Commercialize any product that is directed toward the Collaboration Target, or, in either case, collaborate with a Third Party or grant any Third Party a license, sublicense or other rights to enable any Third Party to do so. Nitto's obligation under this Section 2.5 will not survive after termination or expiration of this Agreement.

2.6 Change of Control. In the event of a Change of Control of Omega during the Term, Omega will provide written notice to Nitto within thirty (30) days of the effective date of such Change of Control.

## ARTICLE 3
## Development; Governance

3.1 Joint Development.

(a) Joint Development Plan. Omega and Nitto will jointly research and Develop the Licensed Product for all human therapeutic, palliative and/or prophylactic applications pursuant to a Joint Development Plan (the "**Joint Development Plan**") setting forth each Party's responsibilities and the Budget for Development of the Licensed Product. The initial Joint Development Plan is attached hereto as Appendix C. Any amendment or modification to the Joint Development Plan is subject to JSC approval.

(b) Project Team. Promptly following the Effective Date, the Parties will establish a Project Team ("**Project Team**"), which shall be responsible for conducting and managing the Joint Development Plan. The Project Team will consist of the development members appointed by each Party, each with experience relevant to such Party's responsibilities under the Joint Development Plan. Each Party will appoint one (1) Research Program Director from the Project Team members, who is a chief member responsible for conducting the Joint Development Plan. Each Party will promptly fill any vacancy created by the resignation or removal of any member appointed by such Party. Either Party may remove and replace any member that it appointed, with or without cause, at any time by prior notice to the other Party.

(c) Subcontracting. Nitto may subcontract any part of its responsibilities to its Affiliates without Omega's consent, and to Third Parties with the consent of Omega, such consent not to be unreasonably withheld. Omega may subcontract any of its responsibilities under the Joint Development Plan to an Affiliate or a Third Party without Nitto's consent; provided, however, Omega will disclose any Third Party subcontractors to Nitto in advance. Within thirty (30) days after subcontracting any of its responsibilities under this Agreement, Nitto will provide notice that includes the identity of such subcontractor, and the activities such subcontractor will be performing; provided, that Omega hereby acknowledges that Nitto will subcontract some parts of its responsibilities to NBPI.

(d) Joint Development Costs. Omega will bear all reasonable costs incurred by Nitto in the Joint Development Plan in accordance with the Budget ("**Nitto's Development Costs**"). Nitto's Development Costs will include, without limitation, cost of materials and the Nitto Materials, NBPI's FTE Costs, project management costs, and Nitto's reasonable expenses related to traveling costs,

accommodation fees and other incidentals that Nitto incurred in the performance of the Joint Development Plan, all in accordance with the Budget. Omega will bear all costs and expenses incurred by Omega through the performance of its responsibilities in the Joint Development Plan.

(e) Discontinuation. Discontinuation of Joint Development is upon expiration of the R&D Term and as provided in Section 3.3(h).

3.2 Alliance Manager.

(a) Alliance Manager. Within thirty (30) days of the Effective Date, each Party will appoint an individual (from such Party or from an Affiliate of such Party) who possesses a general understanding of research issues to act as the facilitator of the meetings of the JSC and the first point of contact between the Parties with regard to questions relating to this Agreement or the overall business relationship and related matters between the Parties (the "**Alliance Managers**"). Each Party may replace its Alliance Manager at any time upon written notice to the other Party. The Alliance Managers:

(i) will use good faith efforts to collaborate, organize and attend all meetings of the JSC, as a non-voting member; and

(ii) may bring any matter to the attention of the JSC where such Alliance Manager reasonably believes that such matter requires attention.

3.3 Joint Steering Committee.

(a) Formation; Composition. Within thirty (30) days of the Effective Date, the Parties will establish a joint steering committee (the "**Joint Steering Committee**" or "**JSC**") comprised of three (3) representatives from each Party (or appointed representatives of an Affiliate of such Party) with sufficient seniority and experience to fulfill the scope of the JSC's responsibilities. Each Party may replace its JSC representatives at any time upon notice to the other Party. The JSC may invite non-members to participate in the discussions and meetings of the JSC. Each meeting of the JSC will be co-chaired by a representative of Nitto and a representative of Omega. The role of the chairpersons will be to convene and preside at meetings of the JSC. The chairpersons will have no additional powers or rights beyond those held by the other JSC representatives. The Alliance Managers will work with the chairpersons to prepare and circulate agendas and to ensure the preparation of minutes.

(b) Specific Responsibilities During the R&D Term. The JSC will, on a Program-by-Program basis:

(i) review and comment on, and oversee the performance of, the Joint Development Plan, and advise on any amendments thereto, including any amendment to the timelines or activities under such Joint Development Plan;

(ii) review and approve, at least once every six (6) months, Nitto's FTE requirements and direct external expenses, including Nitto's project management costs, Nitto's cost of Nitto Materials and other materials, and Nitto's expenses related to traveling costs, accommodation fees and other incidentals that Nitto incurred in the performance of the Joint Development Plan (such approved FTE requirements and expenses, collectively, the "**Budget**");

(iii) select the combination of OEC and Nominated LNP comprising the Licensed Product, and any subsequent combination of OEC and Nominated LNP comprising the Licensed Product which the JSC selects as a replacement for the first such combination for Development;

(iv) establish subcommittees (composed of equal numbers of Omega and Nitto representatives in each subcommittee) to perform specific duties of the JSC, direct each such subcommittee to perform the functions for which it is established, and oversee each subcommittee, including resolution of disputes raised to the JSC by any subcommittee; *provided, however,* that the JSC may expressly delegate certain decision-making authority to a subcommittee within its subject matter expertise; and

(v) perform such other functions as appropriate, to further the purposes of this Agreement, in each case as agreed in writing by the Parties.

(c) Meetings. During the R&D Term, the JSC will meet at least four (4) times per Calendar Year. No later than ten (10) Business Days prior to any meeting of the JSC, the Alliance Managers will jointly prepare and circulate an agenda for such meeting; *provided, however*, that either Party may propose additional topics to be included on such agenda, either prior to or in the course of such meeting. Either Party may also call a special meeting of the JSC (by videoconference, teleconference or in person) by providing at least three (3) Business Days prior notice to the other Party if such Party reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such Party will work with the chairpersons of the JSC to provide the members of the JSC no later than two (2) Business Days prior to the special meeting with an agenda for the meeting and materials reasonably adequate to enable an informed discussion on the matters to be considered. The JSC may meet in person, by videoconference, by teleconference, electronic mail or correspondence, as deemed necessary or appropriate. In-person JSC meetings will be held at locations and on dates and times as mutually agreed upon by Nitto and Omega. At least two (2) JSC representatives from each Party must be present at a meeting of the JSC to have a quorum. Each Party will bear the expense of its respective JSC members' and other representatives in attendance, or for other participation, in JSC meetings, including all travel and related costs and expenses.

(d) Minutes. The Alliance Managers will be responsible for preparing reasonably detailed written minutes of all JSC meetings that reflect topics discussed and action items identified at such meetings. The Alliance Managers will send draft meeting minutes to each member of the JSC for review and approval within twenty (20) Business Days after each JSC meeting. Such minutes will be deemed approved unless one or more members of the JSC objects to the accuracy of such minutes within ten (10) Business Days of receipt. Upon any such objection, the members shall work together in good faith to promptly revise such minutes until such minutes are approved by all members of the JSC. Minutes will be officially endorsed by the JSC at the next JSC meeting.

(e) Decision-Making. During the R&D Term with respect to the Licensed Product, the representatives from each Party on the JSC will have, collectively, one (1) vote on behalf of that Party, and all decision-making will be by consensus. Disputes at the JSC will be handled in accordance with Section 3.3(f).

(f) Resolution of JSC Disputes.

(i) Within the JSC. Subject to the exception specified below in this Section 3.3(f)(ii), all decisions within the JSC will be made by consensus. If the JSC is unable to reach consensus on any issue for which it is responsible, within thirty (30) days after a Party affirmatively states that a decision needs to be made, either Party may elect to submit such issue to the Parties' Executive Officers, in accordance with Section 3.3(f)(ii).

(ii) Referral to Executive Officers. If a Party makes an election under Section 3.3(f)(i) to refer a matter to the Executive Officers, the Executive Officers will use good faith efforts to resolve promptly such matter, which good faith efforts will include at least one (1) in-person, video or telephonic meeting between such Executive Officers within fifteen (15) days after the submission of such

matter to them. If the Executive Officers are unable to reach consensus on any such matter within fifteen (15) days after its submission to them, then Omega's Executive Officer shall have the final decision-making authority, unless such matter relates solely to the Nitto Background Technology, Nitto IP or Nitto Material, and not related to the Licensed Product.

(iii) Good Faith. In conducting themselves on the JSC, and in exercising their rights under this Section 3.3(f), all representatives of both Parties will consider reasonably and in good faith all input received from the other Party. In exercising any decision-making authority granted to it under Section 3.3(e) and this Section 3.3(f), each Party will act based on its good faith judgment taking into consideration the best interests of the Licensed Product and each Party's respective Intellectual Property.

(g) Limitation of JSC Authority. The JSC shall only have the powers expressly assigned to it in this Section 3.3 and elsewhere in this Agreement and shall not have the authority to: (i) modify or amend the terms or conditions of this Agreement; (ii) waive or determine either Party's compliance with the terms or conditions of this Agreement; (iii) decide any issue in a manner that would conflict with the express terms or conditions of this Agreement; or (iv) bind either Party in any way, without prior written consent of such Party. The activities to be performed by the JSC shall solely relate to governance under this Agreement, and are not intended to be or involve the delivery of services.

(h) Discontinuation of the JSC as a Governance Body. Unless the Parties mutually agree to disband the JSC earlier, the JSC shall continue to exist as a governance body with decision-making authority until the end of the R&D Term. Thereafter, the JSC shall have no further responsibilities under this Agreement.

(i) JSC Role after R&D Term. After the expiration of the R&D Term, Omega and not the JSC shall have sole decision-making authority with respect to the Development or Commercialization of the Licensed Product. JSC shall continue solely as a forum for Omega and Nitto to share information and coordinate required activities related to the Development or Commercialization of Licensed Products. For the avoidance of doubt, Nitto shall provide reasonable support as requested by Omega for the Development, manufacture and Commercialization of the Licensed Product throughout the Term; provided, that Omega shall bear Nitto's reasonable costs and expenses, which will include, without limitation, cost of materials, NBPI's FTE Costs, and Nitto's reasonable expenses related to traveling costs, accommodation fees and other incidentals that Nitto incurred in the performance of such support.

3.4 Omega Development and Regulatory Responsibilities. After the R&D Term, Omega will have sole responsibility for and sole authority and decision-making over all regulatory activities for the Licensed Product in the Licensed Territory, both before and after obtaining Marketing Authorization Approval, and shall be responsible for all associated costs and expenses. Omega will have the sole right to conduct all communications with Regulatory Authorities, including all meetings, conferences and discussions (including advisory committee meetings), with regard to the Licensed Product in the Licensed Territory; *provided that*, if Omega reasonably requests that Nitto conduct any communications or otherwise interact with a Regulatory Authority, Nitto will engage in such communications or other interaction with such Regulatory Authority. For the avoidance of doubt, Nitto shall provide reasonable support as requested by Omega for the Development, manufacture and Commercialization of the Licensed Product throughout the Term.

3.5 Commercialization. Omega will have sole authority and responsibility for and sole decision-making over all Commercialization activities for the Licensed Product in the Licensed Territory and will be solely responsible for the associated costs and expenses of such Commercialization activities.

**ARTICLE 4**
**Payments and Royalties**

4.1 Upfront Payment. Within thirty (30) days after the Effective Date ("Initial Payment Date"), in consideration for the rights granted to Omega hereunder, Omega will pay Nitto a one-time, non- refundable upfront payment of One Million United States Dollars (US$1,000,000), wherein such upfront payment will be reduced by and credited against all amounts paid by Omega under the MOU prior to the Effective Date.

4.2 Development Milestone Payments. Omega will make milestone payments (each, a "**Development Milestone Payment**") to Nitto upon the first occurrence of each of the milestone events (each, a "**Development Milestone Event**") by or for Omega or its Affiliates or Sublicensees with respect to the Licensed Product as set forth below in Table 4.2. Omega will notify Nitto of the achievement of each Development Milestone Event within [***] of such achievement. Each Development Milestone Payment will be payable to Nitto by Omega within [***] of the achievement of the specified Development Milestone Event, and such payments when owed or paid will be non-creditable. For clarity, each Development Milestone Payment is payable a maximum of one (1) time only, regardless of the number of Licensed Products to achieve such Development Milestone Event.

**Table 4.2 - Development Milestone Events**

| Development Milestone Event | Development Milestone Payment |
|---|---|
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |

4.3 Sales Milestone Payments. Omega will make milestone payments (each, a "**Sales Milestone Payment**") to Nitto upon cumulative Net Sales of the Licensed Product (each, a "**Sales Milestone Event**") by Omega, its Affiliates or Sublicensees to unaffiliated Third Parties with respect to the first Licensed Product to reach such Sales Milestone Event as set forth below in Table 4.3. Omega will notify Nitto of the achievement of each Sales Milestone Event within forty-five (45) Business Days from the last day of the month of such achievement. Each Sales Milestone Payment will be payable to Nitto by Omega within thirty (30) days after Omega's notification to Nitto of the achievement of the specified Sales Milestone Event, and such payments when owed or paid will be non-creditable. For clarity, each Sales Milestone Payment is payable a maximum of one (1) time only, regardless of the number of Licensed Products to achieve such Sales Milestone Event.

**Table 4.3 - Sales Milestone Events**

| Sales Milestone Event | Sales Milestone Payment |
|---|---|
| [***] | [***] |
| [***] | [***] |

4.4 Royalties.

(a) Net Sales Royalty. Omega will pay to Nitto royalties ("**Royalties**") on a country- by-country basis on worldwide Net Sales for the Licensed Product during the applicable Royalty Term as follows:

(i) In any Calendar Year the worldwide Net Sales on a Licensed Product are less than [***], Omega shall pay Nitto royalties on cumulative worldwide Net Sales from the First Commercial Sale of such Licensed Product at the royalty rates ("**Royalty Rates**") set forth below in Table 4.4, until such cumulative Net Sales reach [***]:

**Table 4.4–Royalty Rates**

| The Portion of Cumulative Net Sales beginning at First Commercial Sale | Royalty Rate |
|---|---|
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |

(ii) In the first Calendar Year the worldwide Net Sales on the Licensed Product are equal to or greater than [***], and every Calendar Year after such Calendar Year, Omega shall pay Nitto a Royalty of [***], regardless of whether cumulative worldwide Net Sales set forth in Section 4.4(a)(i) have achieved the applicable Royalty Rate threshold.

For clarity, once Omega's Royalty obligations for the Licensed Product in a country expire, the Net Sales in such country will be excluded from Royalty calculations (including thresholds and ceilings).

(b) Royalty Adjustments. Royalties will be payable by Omega to Nitto at the royalty rates set forth above on Net Sales, as defined under U.S. Generally Accepted Accounting Principles, of the Licensed Product by Omega, its Affiliates and its Sublicensees to unaffiliated Third Parties during the applicable Royalty Term, subject to the following adjustments.

(i) Third Party Payments. On a country-by-country basis, Omega will be entitled to deduct up to [***] of any payments to Third Parties for Intellectual Property other than Specified IP licensed by Omega, its Affiliates or its sublicensees relating to the Licensed Product that is necessary or useful to Develop, manufacture and/or Commercialize the Licensed Product. Such adjustments in this Section 4.4(b)(i) shall not reduce the Royalty payable to Nitto to less than [***] in any Calendar Quarter; *provided, however*, Omega may carry forward any such adjustment that is not applied as a result of the [***] royalty floor to apply to Royalty payments in subsequent calendar quarters, again subject to such [***] floor, until such adjustment has been applied in full; *provided, further,* on a country-by-country basis, Omega will be entitled to deduct up to [***] of any payments to Third Parties for Specified IP licensed by Omega, its Affiliates or its sublicensees, and in the event a deduction in respect of Specified IP is applied, the royalty floor in this Section 4.4(b)(i) will be reduced to [***] for the duration of the period such payments are made to a Third Party in respect of Specified IP.

(ii) Patent Step-down. In any country and for the period there is no Valid Claim under the Licensed IP, Omega will pay to Nitto [***] of the otherwise applicable Royalty in consideration for the license to Know-How within the Licensed IP.

(c) Royalty Term. The Royalty term ("**Royalty Term**") will be determined on a country-by-country basis and will commence upon the First Commercial Sale in such country and will expire on the last to occur of (i) the expiration of the last to expire Valid Claim within the Licensed IP that Covers the Licensed Product in such country, (ii) expiration of any period of data exclusivity, market exclusivity, or supplemental protection certificates, if any, covering the Licensed Product in the applicable country, and (iii) [***] from the First Commercial Sale of the Licensed Product in such country. Thereafter, Omega's license under Section 2.1 will become irrevocable, perpetual, transferable, sublicensable, fully paid-up and royalty-free on a country-by-country basis.

(d) Blended Royalty. The Parties acknowledge and agree that the Licensed IP licensed under this Agreement may justify Royalty rates or Royalty Terms of differing amounts for the sale of Licensed Product in the Territory. The Parties have determined in light of such considerations and for reasons of mutual convenience that blended Royalty rates for the Licensed IP licensed hereunder will apply during a single Royalty Term for sales of the Licensed Product in the Territory. Consequently, the Parties have agreed to adopt the Royalty rates set forth in this Section 4.4 with respect to the sales of the Licensed Product in the Territory as blended Royalty rates. For the avoidance of doubt, Omega's obligation to pay Royalties under this Section 4.4 is imposed only once at the applicable Royalty rate set forth in this Section 4.4 with respect to the same unit of Licensed Product, notwithstanding that the Licensed Product may be Covered by more than one Valid Claim of a Nitto Patent.

4.5 Payment Terms.

(a) Manner of Payment; Invoices. All amounts specified in this Agreement are in U.S. dollars and all payments to be made by Omega hereunder will be made in U.S. dollars by wire transfer to such bank account as Nitto may designate in advance in writing. All invoices to be delivered to Omega hereunder will be in U.S. dollars and will be delivered in accordance with Section 11.12 or in such other manner specified by Omega from time to time.

(b) Records and Audits. Omega will keep, and will cause each of its Affiliates and Sublicensees, as applicable, to keep adequate books and records of accounting for the purpose of verifying a Milestone Event has been achieved. For the [***] years next following the end of the Calendar Year to which each will pertain, such books and records of accounting of Omega (including those of Omega's Affiliates) will be kept by Omega and will be open for inspection at reasonable times and upon reasonable notice by an independent certified accountant selected by Nitto, and which is reasonably acceptable to Omega, for the sole purpose of inspecting the Milestone Payments due to Nitto under this Agreement. In no event will such inspections be conducted hereunder more frequently than once every [***] or more than once for the same time period. Such accountant must have executed and delivered to Omega and its Affiliates a confidentiality agreement as reasonably requested by Omega, which will include provisions limiting such accountant's disclosure to Nitto to only the results and basis for such results of such inspection. The results of such inspection, if any, will be binding on both Parties absent manifest error. Any payment for a Milestone Event not paid when achieved as determined by the accountant's report will be paid by Omega within thirty (30) days of notification of the results of such inspection. Any Milestone Payment paid but not achieved will be fully creditable against amounts payable in subsequent payment periods, or, upon the request of Omega, paid by Nitto to Omega within thirty (30) days of notification of the results of such inspection. Nitto will pay for such inspections.

(c) Reports and Royalty Payments. Commencing at the beginning of the Royalty Term in a country and for as long as Royalties are due under Section 4.4, Omega will furnish to Nitto a written report for each Calendar Quarter, showing the Net Sales of the Licensed Product and Royalties due for such Calendar Quarter. Reports will be provided within [***] days of the end of the Calendar Quarter for Net Sales generated by Omega and its Affiliates, and within [***] days of the end of the Calendar Quarter for Net Sales generated by Sublicensees. Royalty payments for each Calendar Quarter will be due at the same time as the last such written report for the Calendar Quarter. All such reports will be treated as Confidential Information of Omega.

(d) Currency Exchange. With respect to Net Sales invoiced in U.S. dollars, the Net Sales and the amounts due to Nitto hereunder will be expressed in U.S. dollars. With respect to Net Sales invoiced in a currency other than U.S. dollars, payments will be calculated based on standard methodologies employed by Omega or its Affiliates or Sublicensees for consolidation purposes for the Calendar Quarter for which remittance is made for Royalties.

(e) Taxes. Omega may withhold from payments due to Nitto amounts for payment of any withholding tax that is required by Law to be paid to any taxing authority with respect to such payments. Omega will provide Nitto all relevant documents and correspondence and will also provide to Nitto any other cooperation or assistance on a reasonable basis including proper evidence as to the payment of any such tax, as may be necessary to enable Nitto to claim exemption from such withholding taxes and to receive a refund of such withholding tax or claim a foreign tax credit. The Parties will cooperate with each other in seeking deductions under any double taxation or other similar treaty or agreement from time to time in force. Such cooperation may include Omega making payments from a single source in the U.S., where reasonably possible.

(f) Blocked Payments. In the event that, by reason of applicable Law in any country, it becomes impossible or illegal for Omega or its Affiliates or Sublicensees to transfer, or have transferred

on its behalf, payments owed to Nitto hereunder, Omega will promptly notify Nitto of the conditions preventing such transfer and such payments will be deposited in local currency in the relevant country to the credit of Nitto in a recognized banking institution designated by Nitto or, if none is designated by Nitto within a period of thirty (30) days, in a recognized banking institution selected by Omega or its Affiliate or Sublicensee, as the case may be, and identified in a written notice given to Nitto.

(g) Interest Due. If any payment due to Nitto under this Agreement is overdue (and is not subject to a good faith dispute), then Omega will pay interest thereon (before and after any judgment) at monthly rate of the lesser of [***], and the maximum rate permitted by applicable Law, such interest to run from the date upon which payment of such sum became due until payment thereof in full together with such interest.

## ARTICLE 5
## Ownership and Inventorship of IP

5.1 Ownership. As between the Parties, (a) Nitto will own and retain all right, title and interest in and to the Nitto Background Technology, Nitto IP and Nitto Materials, (b) Omega will own and retain all right, title and interest in and to the Omega Background Technology, Omega IP and Omega Materials, and each Party with have an undivided one-half (1/2) interest in and to the Joint IP and Modified Material. Notwithstanding the foregoing, without the prior written consent of the other Party, neither Party will use the Joint IP for any purpose, other than under the Joint Development Plan, or otherwise for Omega Developing, manufacturing and Commercializing the Licensed Product under this Agreement.

5.2 Assignments of Other Party's IP.

(a) Nitto IP. Omega, for itself and on behalf of its Affiliates, licensees and Sublicensees, and employees, subcontractors, consultants and agents of any of the foregoing, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign), to Nitto all Omega's right, title and interest in and to the Nitto IP. Omega will reasonably cooperate, and will cause the foregoing Persons and entities to reasonably cooperate, with Nitto to effectuate and perfect the foregoing ownership, including by promptly executing and recording assignments and other documents consistent with such ownership.

(b) Omega IP. Nitto, for itself and on behalf of its Affiliates, licensees and Sublicensees, and employees, subcontractors, consultants and agents of any of the foregoing, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign), to Omega all Nitto's right, title and interest in and to the Omega IP. Nitto will reasonably cooperate, and will cause the foregoing Persons and entities to reasonably cooperate, with Omega to effectuate and perfect the foregoing ownership, including by promptly executing and recording assignments and other documents consistent with such ownership.

(c) Joint IP. Each Party, for itself and on behalf of its Affiliates, licensees and sublicensees, and employees, subcontractors, consultants and agents of any of the foregoing, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign), to the other Party a joint and undivided one-half (1/2) ownership interest in and to all Joint IP.

## ARTICLE 6
## Patent Prosecution and Maintenance

6.1 Filing of Patents Covering Program IP Generally. Neither Party will file any applications for patents or trademarks claiming the Joint IP, Omega IP or Nitto IP until the Parties meet and

agree upon the timing of such filings. Furthermore, Nitto and Omega will discuss filings of any patent applications claiming the Joint IP, Omega IP or Nitto IP after the JSC makes a decision on combination of a specific Omega Material with the specific Nitto Material as a Licensed Product under this Agreement, unless otherwise agreed upon by the Parties through mutual written consent.

6.2 Nitto Patents.

(a) Prosecution and Maintenance. As between the Parties and subject to Sections 6.1 and 6.2(b), Nitto will have the sole right, at its sole cost, to file, prosecute and maintain Nitto Patents.

(b) Election Not to Prosecute or Maintain or Pay Patent Costs. If Nitto elects not (i) to file, prosecute or maintain any Nitto Patents for which it is responsible under this Section 6.2 in any particular country before the applicable filing deadline or continue such activities once filed in a particular country, or (ii) to pay the Patent Costs associated with prosecution or maintenance of any such Nitto Patents, then in each such case Nitto will so notify Omega, promptly in writing and in good time to enable Omega to meet any deadlines by which an action must be taken to preserve such Nitto Patent in such country. Upon receipt of each such notice by Nitto, Omega will have the right, but not the obligation, to decide whether to obtain, and to seek, prosecute and maintain such Nitto Patents and to take any necessary actions without losing patent protection, and Omega will have the right (but not the obligation), to file, prosecute and maintain in any country such Nitto Patent in the sole name of Omega, at Omega's sole cost. If Omega elects to obtain, and to seek, prosecute and maintain such Nitto Patents, Nitto will make available to Omega its documentation, and its authorized attorneys, agents or representatives, and such of its employees, as are reasonably necessary to assist Omega in obtaining and maintaining Nitto Patents and the patent protection described under this Section 6.4(b). Nitto will sign or have signed, all legal documents and instruments, and take such further actions necessary to file and prosecute such patent applications in order for Omega to obtain or maintain such Nitto Patents.

6.3 Omega Patents.

(a) Filing, Prosecution and Maintenance. As between the Parties and subject to Section 6.1, Omega will have the sole right, at its sole cost, to file, prosecute and maintain Omega Patents.

6.4 Joint Patents.

(a) Filing, Prosecution and Maintenance. As between the Parties and subject to Section 6.1, and Omega will have the sole right, at its sole cost, to file, prosecute and maintain Joint Patents; provided, that Omega will give Nitto reasonable opportunity to comment on type and scope of claims, patent application documents and all other material aspects of the preparation, filing, prosecution and maintenance of the Joint Patents (including without limitation, filing date), and fully inform Nitto of the progress of any material events with respect to the filing, prosecution and maintenance of the Joint Patents (including without limitation, completion of filing, entering PCT national phase and registration of the Joint Patents).

(b) Nitto Step-In Right. In the event that Omega elects not to file or continue to prosecute or maintain patent protection on any Joint Patent, Omega will notify Nitto of such decision in sufficient time so as to permit Nitto to decide whether to obtain Omega's interest in such Joint Patents, and to seek, prosecute and maintain such Patent and to take any necessary actions without losing patent protection, and Nitto will have the right (but not the obligation), to file, prosecute and maintain in any country such Joint Patent in the sole name of Nitto, at Nitto's sole cost. Omega will make available to Nitto its documentation, and its authorized attorneys, agents or representatives, and such of its employees, as are reasonably necessary to assist Nitto in obtaining and maintaining Omega's interest and the patent protection

described under this Section 6.4(b). Omega will sign or have signed, all legal documents necessary to file and prosecute such patent applications or to obtain Omega's interest in or maintain such Joint Patents.

6.5 Regulatory Exclusivity Periods. With respect to any Patent term extension, supplemental protection certificate or any other Patent listing or extension with respect to any Nitto Patent or Joint Patent Covering the Licensed Product, the Parties will discuss and seek to reach mutual agreement, subject to applicable Law, on whether and which Nitto Patent or Joint Patent will be subject to such action, and once such agreement is reached, Nitto will cooperate with such action. Except where required under applicable Law, without the written consent of Omega, Nitto will not apply for, and is not authorized under this Agreement to apply for, any Patent term extension, supplemental protection certificate or any other Patent listing or extension required for any regulatory exclusivity periods for the Licensed Product. For the avoidance of doubt, Nitto is not restricted from applying for any Patent term extension, supplemental protection certificate or any other Patent listing or extension required for any regulatory exclusivity periods for any product but the Licensed Product.

6.6 Patent Listings. Omega will have the sole right, in its sole discretion, to make all filings with Regulatory Authorities in the Territory for the Licensed Product in the FDA's Orange Book or Purple Book or in response to a biosimilar application under Section 351(k) of the Public Health Service Act, and under any similar or equivalent Laws in other countries or jurisdictions.

6.7 Cooperation. Each Party will reasonably cooperate with the other Party in those activities involving the Nitto Patents or the Joint Patents set forth in Sections 6.1 to 6.6. Such cooperation includes promptly executing all documents, or requiring inventors, subcontractors, employees and consultants and agents of Omega and Nitto and their respective Affiliates and Sublicensees to execute all documents, as reasonable and appropriate so as to enable such activities in respect of any such Nitto Patents, Omega Patents or Joint Patents, as the case may be, in any country.

## ARTICLE 7
## Patent Enforcement and Defense

7.1 Notice. To the extent not in breach of an obligation of confidentiality, each Party will promptly notify the other Party, in writing upon learning of any actual or suspected infringement of any Nitto Patents or Joint Patents by a Third Party, or of any claim of invalidity, unenforceability, or non- infringement of any Nitto Patents or Joint Patents, in each case to the extent such infringing, unauthorized or misappropriating activities involve, as to the Licensed Product, a Competing Product in the Licensed Field ("**Competitive Infringement**"), and will, along with such notice, supply the other Party with any evidence in its possession pertaining thereto.

7.2 Enforcement and Defense.

(a) Enforcement.

(i) As between the Parties, Nitto will have the first right, but not the obligation, at its sole cost to seek to abate any infringement of the Nitto Patents by a Third Party, or to file suit against any such Third Party for such infringement. If Nitto elects not to exercise its first right to take action or to bring suit to prosecute such infringement or to continue such action or suit, it will notify Omega in writing of such election within thirty (30) days after becoming aware of or receipt of the notice of the infringement or within fifteen (15) days after the election to stop any such action or suit, as applicable. If after the expiration of the thirty (30) day period (or, if earlier, the date upon which Nitto provides written notice that it does not plan to bring such action), Nitto has neither obtained a discontinuance of infringement nor filed suit against any such Third Party infringer of such Patent, or in the case of an election by Nitto not

to continue to prosecute an infringement of an Nitto Patent, Omega will have the right, but not the obligation, to take action or bring suit against such Third Party infringer of Nitto Patents to the extent the Nitto Patents are necessary or useful for the research, Development, manufacturing and Commercialization of the Licensed Product but not necessary or useful for the research, Development, manufacturing or Commercialization of any other LNP comprising product covered by such Nitto Patent that is licensed or optioned by Nitto to a Third Party or is under Late-Stage Development by Nitto, *provided that* Omega will bear all of the expense of such action or suit that it brings against such Third Party infringer.

(ii) As between the Parties, Nitto will have the right, but not the obligation, at its sole cost to seek to abate any infringement of the Joint Patents by a Third Party, or to file suit against any such Third Party for such infringement, if such infringement is with respect to the Nitto IP and not a Competitive Infringement. As between the Parties, Omega will have the sole right, but not the obligation, at its sole cost to seek to abate any infringement of the Joint Patents by a Third Party, or to file suit against any such Third Party for a Competitive Infringement, with respect to which Omega will consider Nitto's input in good faith.

(iii) Except as expressly provided under Section 7.2(a)(ii), neither Party will seek to abate any infringement of the Joint Patents by a Third Party, or file suit against any such Third Party for such infringement, without the prior written consent of the other Party. For clarity, Omega will have the sole right to enforce any Patents Controlled by Omega other than the Nitto Patents and the Joint Patents.

(b) Defense.

(i) As between the Parties, Nitto will have the first right, but not the obligation, at its sole cost, to defend against a declaratory judgment action or other action to the extent challenging the validity or enforceability of any Nitto Patent. Omega will have the right but not the obligation, at its sole cost, to defend against any other declaratory judgment action or other action challenging any Nitto Patent that, on the date of first notice of such action, are not necessary or useful for the research, Development, manufacturing and Commercialization of any lipid nanoparticle comprising product that is licensed or optioned by Nitto to a Third Party or is under Late-Stage Development by Nitto. If Nitto does not take steps to defend within a reasonable time, or elects not to continue any such defense (in which case it will promptly provide notice thereof to Omega), then Omega will have the right, but not the obligation, to defend any Nitto Patents that cover the Licensed Product and no other product licensed or optioned by Nitto to a Third Party or commercialized by Nitto; *provided, however that* Omega will bear all the expenses of such suit. If a Third Party files a declaratory judgment or other action challenging any Joint Patent, the Parties will reasonably cooperate in good faith to determine each Party's responsibility with respect to the defense of such declaratory judgment or other action. Notwithstanding the foregoing, any response to a Third Party infringer's counterclaim of invalidity or unenforceability of any Nitto Patents or Joint Patents will be controlled by the Party who controls the relevant enforcement proceeding pursuant to Section 7.2(a) unless otherwise mutually agreed by the Parties. For clarity, Omega will have the sole right to defend any Patents Controlled by Omega other than the Nitto Patents.

(ii) In the event that any action, suit or proceeding is brought against either Party or an Affiliate of either Party, or a Sublicensee of Omega or its Affiliates, alleging the infringement of the Patents or Know-How of a Third Party by the research, Development, manufacture, use, sale, import, export, Commercialization or exploitation of the Licensed Product, such Party will promptly notify the other Party within five (5) Business Days of the earlier of (A) receipt of service of process in such action, suit or proceeding, or (B) the date such Party becomes aware that such action, suit or proceeding has been instituted; *provided*, that the foregoing obligation to notify Nitto will only apply if the alleged infringement relates to Nitto IP or Joint IP. Except as set forth in Section 7.2(b)(i), Omega will have the right, but not the obligation, to defend such action, suit or proceeding in the Territory at its sole cost.

(c) Withdrawal, Cooperation and Participation. With respect to any infringement or defensive action identified above in this Section 7.2 which may be controlled by either Omega or Nitto:

(i) The non-controlling Party will cooperate with the Party controlling any such action (as may be reasonably requested by the controlling Party), including by (A) providing access to relevant documents and other evidence, (B) making its and its Affiliates and Sublicensees and all of their respective employees, subcontractors, consultants and agents available at reasonable business hours and for reasonable periods of time, but only to the extent relevant to such action, and (C) if necessary, being joined as a party, subject for this clause (C) to the controlling Party agreeing to indemnify such non-controlling Party for its involvement as a named party in such action and paying those Losses incurred by such Party in connection with such joinder, but subject in all respects to the indemnification obligations of Section 9.6. The Party controlling any such action will keep the other Party updated with respect to any such action, including providing copies of all documents received or filed in connection with any such action.

(ii) Each Party will have the right to participate or otherwise be involved in any such action controlled by the other Party, in each case at the participating (*i.e.*, non-controlling) Party's sole cost and expense. If a Party elects to so participate or be involved, the controlling Party will provide the participating Party and its counsel with an opportunity to consult with the controlling Party and its counsel regarding the prosecution of such action (including reviewing the contents of any correspondence, legal papers or other documents related thereto), and the controlling Party will take into account reasonable requests of the participating Party regarding such enforcement or defense. The foregoing will not apply to any defensive actions described in Section 7.2(b)(ii) that do not involve claims specifically relating to a Nitto or Joint Patent.

(d) Settlement. Neither Party will settle or consent to an adverse judgment in any action described in this Section 7.2 and controlled by such Party, including any judgment which affects the scope, validity or enforcement of any Nitto Patents or Joint Patents involved therewith, without the prior written consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed); *provided*, that the foregoing will not apply to the extent that such settlement or consent to an adverse judgment does not relate to an Nitto Patent or Joint Patent.

(e) Damages. Unless otherwise agreed by the Parties, all monies recovered upon the final judgment or settlement of any action which may be controlled by either Omega or Nitto and described in Section 7.2(a) or 7.2(b) in each case will be used first to reimburse the controlling Party, and thereafter the non-controlling Party, for each of their out-of-pocket costs and expenses relating to the action. With respect to the balance of any such recovery, Omega will retain such recovery, less the amount of Royalties payable to Nitto by treating such amounts as "Net Sales" hereunder.

7.3 Patent Challenges.

(a) Consequences of Challenge. If Omega or any of its Affiliates, licensees, or Sublicensees (or any Person acting on its or their behalf) brings or files a claim, action or proceeding (including without limitation in a patent office, court, administrative agency or other forum), or assists, requests or affirmatively supports any Third Party in bringing or filing such a claim, action or proceeding, to challenge the validity or enforceability of any of the Patents within the Nitto Background Technology or Nitto IP (or otherwise within the Licensed IP other than Joint Patents) in any jurisdiction where such Patent exist, Nitto may, at its option and upon written notice terminate the licenses granted hereunder with respect to such challenged Patents in all jurisdictions. If following such a challenge, Nitto elects to terminate the licenses, but is finally determined in a Major Market Country that the remedy of termination of the licenses to such Patent is not enforceable (after exhaustion of all available appeals, unless an appeal is not available), the license to such challenged Patents in all jurisdictions shall not terminate, and instead Omega shall pay

(and as applicable shall cause its Affiliates, licensees and Sublicensees to pay) Nitto (i) Nitto's documented costs and expenses incurred as a result of defending, responding to, or addressing any such claim, action, or proceeding regarding the validity or enforceability of such challenged Patent, including without limitation all attorney's fees and legal and court costs and expenses incurred by Nitto (within thirty (30) days of Nitto's invoice therefor), and (ii) Milestone Payments and Royalties payable by Omega to Nitto hereunder as of the date of such claim, action, or proceeding initiated by a factor of two times (2x) the amount of such Milestone Payments and Royalties that would otherwise be due (so that all such Milestone Payments and Royalties are thereupon doubled under this Agreement), until final resolution, withdrawal or other cessation of such challenge.

(b) Notwithstanding the foregoing, the provisions of Section 7.3(a) shall not apply in the event Omega or its Affiliate, licensee, Sublicensee or a Third Party challenges the validity or enforceability of a Nitto Patent as a counterclaim to a claim, action or proceeding initially brought by or on behalf of Nitto, an Affiliate or a sublicensee of Nitto against Omega or such other Person for infringement of such Nitto Patent, or in the event Omega or such other Person is forcefully joined by a Third Party to a challenge of such Nitto Patent as a necessary party to a counterclaim to a claim, action, or proceeding challenging such Nitto Patent, Omega or such other Person has exhausted all reasonable legal means of avoiding such joinder, and Omega or its Affiliates or Sublicensees or licensees has not initiated, suggested, supported, directed, encouraged, or requested the Third Party to challenge the Nitto Patent.

(c) In the event any remedy described in Section 7.3(a) above is invalid or unenforceable, then such invalid or unenforceable remedy shall be severed from this Agreement, and any enforceable remedy shall be available to Nitto and the rest of this Article 7 shall remain in full force and effect.

## ARTICLE 8
## Confidentiality

8.1 Confidential Information. Each Party ("**Disclosing Party**") may disclose to the other Party ("**Receiving Party**") and Receiving Party may acquire during the course and conduct of activities under this Agreement, certain non-public confidential information of Disclosing Party in connection with this Agreement. The term "**Confidential Information**" means all information of any kind, whether in written, oral, graphical, machine-readable or other form, whether or not marked as confidential or proprietary, that is disclosed or made available by or on behalf of the Disclosing Party to or on behalf of the Receiving Party in connection with this Agreement. For the avoidance of doubt, except as otherwise set forth in this Agreement, Confidential Information (as such term is defined in the MDA) relating to the Licensed Product that is disclosed or made available by or on behalf of the Disclosing Party to the Receiving Party in connection with or under the MDA remains subject to the confidentiality and non-use provisions of the MDA.

8.2 Restrictions. During the Term and for five (5) years thereafter, or with respect to any trade secret included in the Confidential Information for so long as such trade secret is protected under applicable Laws (*provided*, that Receiving Party has not publicly disclosed such trade secret in breach of its obligations under this Article 8), Receiving Party will keep all Disclosing Party's Confidential Information in confidence with the same degree of care with which Receiving Party holds its own confidential information, but in no event less than reasonable care. Receiving Party will not use Disclosing Party's Confidential Information except for in connection with the performance of its obligations and exercise of its rights under this Agreement. Receiving Party has the right to disclose Disclosing Party's Confidential Information without Disclosing Party's prior written consent to Receiving Party's Affiliates, and each of their employees, subcontractors, consultants and agents who have a need to know such Confidential Information in order to perform (or for such entities to determine their interest in performing)

Receiving Party's obligations and exercise their rights under this Agreement and who are under written obligation to comply with the restrictions on use and disclosure that are no less restrictive than those set forth in this Article 8. Receiving Party assumes responsibility for such Persons maintaining Disclosing Party's Confidential Information in confidence and using same only for the purposes described herein.

8.3 Exceptions. Receiving Party's obligation of nondisclosure and the limitations upon the right to use the Disclosing Party's Confidential Information will not apply to a specific portion of the Disclosing Party's Confidential Information to the extent that Receiving Party can demonstrate that such portion: (a) was known to Receiving Party or any of its Affiliates prior to the time of disclosure by the Disclosing Party without obligation of confidentiality; (b) is or becomes public knowledge through no fault or omission of Receiving Party or any of its Affiliates; (c) is obtained on a non-confidential basis by Receiving Party or any of its Affiliates from a Third Party who to Receiving Party's knowledge is lawfully in possession thereof and under no obligation of confidentiality to Disclosing Party; or (d) has been independently developed by or on behalf of Receiving Party or any of its Affiliates without the aid, application or use of Disclosing Party's Confidential Information.

8.4 Permitted Disclosures. Subject to Section 8.3, Receiving Party may disclose Disclosing Party's Confidential Information to the extent (and only to the extent) such disclosure is permitted under Section 8.2 or is reasonably necessary in the following instances:

(a) in order and to the extent required to comply with applicable Laws (including any securities Laws or regulations or the rules of a securities exchange applicable to Receiving Party) or with a legal or administrative proceeding or as required by a court or administrative order;

(b) in connection with prosecuting or defending litigation, including responding to a subpoena in a Third Party litigation;

(c) in connection with filing, prosecuting and enforcing Patents in connection with Receiving Party's rights and obligations pursuant to this Agreement;

(d) to actual and potential acquirers, assignees, investment bankers, investors, lenders and other financing sources, and to consultants and advisors of the Receiving Party; and

(e) in the case of Omega, to (i) subcontractors, (ii) licensees, Sublicensees, assignees and collaboration partners, or (iii) potential and actual licensees, Sublicensees, assignees, collaboration or strategic partners or acquirors but in case (iii) only such information that is reasonably necessary or useful for the potential licensee, Sublicensee, assignee or collaboration partner to evaluate the Licensed Product and its manufacturing processes, including the particular chemical structure and formulation of any lipid nanoparticles incorporated in such products.

Where reasonably possible, Receiving Party will notify Disclosing Party of Receiving Party's intent to make any disclosure pursuant to subsections (a) and (b) above sufficiently prior to making such disclosure so as to allow Disclosing Party adequate time to take whatever action it may deem appropriate to protect the confidentiality of the information to be disclosed. Moreover, with respect to subsections (d) and (e) above, each of those entities will be required to comply with the restrictions on use and disclosure in Section 8.2 (other than investment bankers, investors, lenders, and other financing sources which must be bound prior to disclosure by commercially reasonable obligations of confidentiality). Confidential Information that is required to be disclosed pursuant to subsections (a) or (b) above will remain otherwise subject to the confidentiality and non-use provisions of Sections 8.1 and 8.2. If either Party concludes that a copy of this Agreement must be filed with the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States, at least twenty (20) days in advance of

any such filing such Party will provide the other Party with a copy of this Agreement showing any provisions hereof as to which the Party proposes to request confidential treatment, will provide the other Party with a reasonable opportunity to comment on any such proposed redactions and to suggest additional redactions, and will take such Party's reasonable and timely comments into consideration before so filing this Agreement.

8.5 Return of Confidential Information. Upon expiry or earlier termination of this Agreement, upon written request of a Party (such request, if made, to be made within three (3) months of such expiry or termination) the other Party will destroy or return (as will be specified in such request) to the requesting Party all copies of the Confidential Information of the requesting Party; *provided*, that a Party may retain: (a) one copy of such Confidential Information for record-keeping purposes, for the sole purpose of ensuring compliance with this Agreement; (b) any copies of such Confidential Information as is required to be retained under applicable Laws; and (c) any copies of any computer records and files containing Confidential Information that have been created by such Party's routine archiving/backup procedures, in each case, *provided that* such copies are maintained in accordance with this Article 8.

8.6 Publications.

(a) Notwithstanding anything in this Agreement or the MDA to the contrary, Omega is permitted to publish the results of its Development and other activities under this Agreement, *provided, however*, that if Omega wishes to make a publication or public presentation of such results that contains the Confidential Information of Nitto, Omega will deliver to Nitto a copy of any proposed written publication or presentation of such results at least thirty (30) days prior to submission for publication or presentation. Nitto will have the right (i) to propose modifications to the publication or presentation for patent reasons, trade secret reasons or business reasons within ten (10) days of receipt of such copy, which proposals Omega will consider in good faith, except to the extent such proposed modification involves the protection of Nitto's Confidential Information, other than Confidential Information that is Study Data generated in the performance of a Work Plan or Joint Development Plan under the MDA (which is Confidential Information of both Nitto and Omega), in which case Omega shall implement such proposal, and (ii) to request a reasonable delay in publication or presentation in order to protect patentable information in accordance with Article 6. Following the expiration of the applicable time period for review (and subject to the implementation of Nitto's proposed modifications as provided for above), Omega will be free to submit for publication or otherwise disclose to the public such results, subject to the procedures set forth in the remainder of this Section 8.6. If Nitto provides written notice to Omega requesting a delay pursuant to clause (ii) in this Section 8.6, Omega will delay such submission or presentation for a period of an additional forty five (45) days to enable Nitto to file patent applications on the disclosed subject matter. Omega will thereafter be free to publish or disclose such information, except that Omega may not disclose any Confidential Information of Nitto in violation of Section 8.2. Omega will comply with standard academic practice regarding authorship of scientific publications and recognition of the contributions of other parties in any scientific publications. For avoidance of doubt, Nitto shall not be permitted to publish any Study Data, or other similar information and data discovered, generated, made or reduced to practice in the performance of this Agreement, the Joint Development Plan, or the MDA specific to the Collaboration Target.

(b) Nitto shall be permitted to publish any information Controlled by Nitto related to the Nitto Materials and Nitto Background Technology that do not reference or incorporate Modified Materials, Omega Materials, Omega Background Technology, Omega's Confidential Information or Omega IP.

(c) Omega shall be permitted to publish any information Controlled by Omega related to the Omega Materials and Omega Background Technology to do not reference or incorporate any Nitto

Materials, Nitto Background Technology or Nitto's Confidential Information. Any publication that references or incorporates Modified Materials, Nitto Materials, Nitto Background Technology or Nitto IP shall be subject to the provisions of Section 8.6(a).

8.7 Terms of this Agreement; Publicity. The Parties agree that the existence and terms of the Parties' relationship and this Agreement will be treated as Confidential Information of both Parties, and thus may be disclosed only as permitted by Sections 8.2 or 8.4. Except as required by applicable Laws (including any securities Laws or the regulations or rules of a securities exchange) or otherwise agreed by the Parties in writing, each Party agrees not to issue any press release or public statement disclosing information relating to the existence of this Agreement or the transactions contemplated hereby or the terms hereof without the prior written consent of the other Party.

## ARTICLE 9
## Warranties; Limitations of Liability; Indemnification

9.1 Representations and Warranties. Each Party represents and warrants to the other as of the MOU Effective Date and the Effective Date that:

(a) it is a corporation duly organized, validly existing, and in good standing under the Laws of the jurisdiction in which it is incorporated,

(b) it has the legal right and power to enter into this Agreement, to extend the rights and licenses granted or to be granted to the other in this Agreement, and to fully perform its obligations hereunder,

(c) it has taken all necessary corporate action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder,

(d) this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms, limited by applicable bankruptcy, insolvency, reorganization, moratorium and other Laws of general application affecting the enforcement of creditors' rights generally and as may be limited by Laws relating to the availability of specific performance, injunctive relief or other equitable remedies,

(e) the execution, delivery and performance of this Agreement by such Party does not violate any Law of any court, governmental body or administrative or other agency having jurisdiction over such Party,

(f) no government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any applicable Laws currently in effect, is necessary for the transactions contemplated by this Agreement or for the performance of its obligations under this Agreement, and

(g) during the Term, that its Affiliates, its and their employees, and their consultants and agents have executed agreements or have existing obligations under Law requiring assignment to such Party of all intellectual property and proprietary rights made during the course of and as the result of their activities in connection with this Agreement, and obligating such individuals to maintain as confidential the Confidential Information of a Disclosing Party under the MDA or this Agreement, and of any Third Party which such Party may receive.

9.2 Additional Representations of Nitto. Nitto hereby represents and warrants to Omega as of the MOU Effective Date and the Effective Date as follows:

(a) Impairment. Neither Nitto nor any of its Affiliates has entered into any agreement or otherwise licensed, granted, assigned, transferred, conveyed or otherwise encumbered or disposed of any right, title or interest in or to any of its assets, including any Licensed IP, that would in any way conflict with or impair the scope of any rights or licenses granted to Omega hereunder.

(b) Patents and Know-How. Appendix A sets forth a complete and accurate list of all Nitto Patents and Patents within the Nitto Background Technology as of the Effective Date. Nitto is the sole and exclusive owner of the Licensed IP, or otherwise has the right to license the Licensed IP and grant rights to Omega as set forth in this Agreement as of the MOU Effective Date and the Effective Date. All Nitto inventors of the Licensed IP have validly assigned their rights to the Licensed IP to Nitto. Nitto is and will remain entitled to grant to Omega the licenses and rights specified or contemplated by this Agreement, to the Patents and the Know-How within the Licensed IP. To Nitto's knowledge, the Nitto Patents have been diligently prosecuted and maintained in accordance with applicable Laws. None of the Nitto Patents are or have been involved in any opposition, cancellation, interference, reissue or reexamination proceeding, and to Nitto's knowledge as of the MOU Effective Date and the Effective Date, no Licensed IP is the subject of any judicial, administrative or arbitral order, award, decree, injunction, lawsuit, proceeding or stipulation. Neither Nitto nor any of its Affiliates has received any notice alleging that the Nitto Patents are invalid or unenforceable or challenging Nitto's ownership of or right to use the Licensed IP. For the avoidance of doubt, except for the representations contained in this Section 9.2(b), Nitto does not represent or warrant otherwise the validity of the Licensed IP and makes no representations or warranties whatsoever with regard to the scope of the Licensed IP, or that the Licensed IP may be exploited by Omega, its Affiliates or Sublicensees without infringing other patents or other intellectual property rights of Third Party.

(c) Entire LNP IP. The Intellectual Property licensed to Omega under this Agreement comprises all Intellectual Property that Nitto owns or has rights under or to that are or may be reasonably necessary or useful for the production, use, research, Development, manufacture or Commercialization of the Licensed Product.

(d) Encumbrances. Nitto and its Affiliates are not subject to any payment obligations to Third Parties as a result of the execution or performance of this Agreement. Neither Nitto nor any of its Affiliates has granted any liens or security interests on the Licensed IP, and the Licensed IP are free and clear of any mortgage, pledge, claim, security interest, covenant, easement, encumbrance, lien or charge of any kind.

(e) Defaults. The execution, delivery and performance by Nitto of this Agreement and the consummation of the transactions contemplated hereby will not result in any violation of, conflict with, result in a breach of or constitute a default under any understanding, contract or agreement to which Nitto is a party or by which it is bound, in each case as would reasonably be expected to have a material adverse effect on the rights granted to Omega hereunder.

(f) Litigation. There is no action, suit, proceeding or investigation pending or, to the knowledge of Nitto, currently threatened in writing against or affecting Nitto that questions the validity of this Agreement, the right of Nitto to enter into Agreement or consummate the transactions contemplated hereby or that relates to the Licensed IP.

(g) Infringement. Neither Nitto nor any of its Affiliates has received any notice of any claim, nor does Nitto or its Affiliates have any knowledge of any reasonable basis for any claim, that any

Patent, Know-How or other Intellectual Property owned or controlled by a Third Party, but except for the Specified IP, would be infringed or misappropriated by the practice of any Licensed IP or the Joint IP in connection with the production, use, research, Development, manufacture or Commercialization of the Licensed Product. For the avoidance of doubt, neither Nitto nor any of its Affiliates make any representations and warranties with respect to non-infringement and no-misappropriation of the Specified IP by the practice of any Licensed IP or the Joint IP in connection with the production, use, research, Development, manufacture or Commercialization of the Licensed Product.

(h) Third Party Infringement. To Nitto's knowledge, no Third Party is infringing or has infringed any Patent within the Licensed IP or is misappropriating or has misappropriated any Know- How within the Licensed IP.

(i) No Debarment. Neither Nitto nor any of its Affiliates, nor its or their respective employees, have been Debarred or are subject to Debarment.

9.3 Disclaimers. Without limiting the respective rights and obligations of the Parties expressly set forth herein, each Party specifically disclaims any guarantee that the Licensed Product will be successful, in whole or in part or that it does not infringe on any Third Party Intellectual Property. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, THE PARTIES MAKE NO REPRESENTATIONS AND EXTEND NO WARRANTY OF ANY KIND UNDER THIS AGREEMENT, EITHER EXPRESS OR IMPLIED.

9.4 No Consequential Damages. NOTWITHSTANDING ANYTHING IN THIS LICENSE AGREEMENT OR OTHERWISE, NEITHER PARTY WILL BE LIABLE TO THE OTHER OR ANY THIRD-PARTY WITH RESPECT TO ANY SUBJECT MATTER OF THIS AGREEMENT FOR ANY INDIRECT, PUNITIVE, SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES (INCLUDING, WITHOUT LIMITATION, LOSS OF REVENUES OR PROFITS, LOSS OF USE, COST OF REPLACEMENT, COST OF CAPITAL AND CLAIMS OF CUSTOMERS, INTEREST CHARGES, OR ANY INCREASED COSTS, UNLESS IN EACH CASE AN ARBITRATOR OR A COURT OF LAW DETERMINES SUCH DAMAGES TO BE DIRECT DAMAGES); *PROVIDED THAT* THIS SECTION 9.4 WILL NOT APPLY TO BREACHES OF A PARTY'S OBLIGATIONS UNDER ARTICLE 8 OR THE PARTIES' INDEMNIFICATION RIGHTS AND OBLIGATIONS UNDER SECTION 9.6.

9.5 Performance by Others. The Parties recognize that each Party may perform some or all of its obligations under this Agreement through Affiliates and Third Party agents; *provided, however*, that each Party will remain responsible and liable for the performance by its Affiliates and Third Party agents and will cause its Affiliates and Third Party agents to comply with the applicable provisions of this Agreement in connection therewith.

9.6 Indemnification.

(a) Indemnification by Omega. Omega will indemnify Nitto, its Affiliates and their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (collectively, "**Nitto Indemnitees**"), and defend and hold each of them harmless, from and against any and all losses, damages, liabilities, costs and expenses (including reasonable attorneys' fees and expenses) (collectively, "**Losses**") in connection with any and all suits, investigations, claims or demands of Third Parties (collectively, "**Third Party Claims**") against the Nitto Indemnitees to the extent arising from or occurring as a result of: (i) the breach by Omega of any provision of this Agreement; (ii) any negligence or willful misconduct on the part of any Omega Indemnitee in connection with this Agreement; (iii) the final decision made by Omega's Executive Officer pursuant to Section 3.3(f)(ii) with respect to any matter that

the JSC is unable to reach consensus; or (iv) the Development, manufacture or Commercialization by or on behalf of Omega or any of its Affiliates or Sublicensees of the Licensed Product other than if solely related to any Nitto Materials, Nitto IP or component thereof (unless due to the manufacture of any of the foregoing by a Person other than Nitto).

(b) Indemnification by Nitto. Nitto will indemnify Omega, its Affiliates and their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (collectively, "**Omega Indemnitees**"), and defend and hold each of them harmless, from and against any and all Losses in connection with any and all Third Party Claims against Omega Indemnitees to the extent arising from or occurring as a result of: (i) the breach by Nitto of any provision of this Agreement; or (ii) any negligence or willful misconduct on the part of any Nitto Indemnitee in connection with this Agreement.

(c) Notice of Claim. All indemnification claims provided for in Sections 9.6(a) and 9.6(b) will be made solely by such Party to this Agreement (the "**Indemnified Party**"). The Indemnified Party will promptly notify the Indemnifying Party (the "**Indemnifying Party**") in writing of any Losses or the discovery of any fact upon which the Indemnified Party intends to base a request for indemnification under Section 9.6(a) and 9.6(b) (each such notice, an "**Indemnification Claim Notice**"), *provided that* the failure to promptly provide such notice and details will not relieve the Indemnifying Party of any of its indemnification obligations hereunder except to the extent that the Indemnifying Party's defense of the relevant Third Party Claim is prejudiced by such failure. Each Indemnification Claim Notice must contain a description of the claim and the nature and estimated amount of such Loss (to the extent that the nature and amount of such Loss is known at such time). The Indemnified Party will furnish promptly to the Indemnifying Party copies of all papers and official documents received in respect of any Losses and Third Party Claims.

(d) Defense, Settlement, Cooperation and Expenses.

(i) Control of Defense. At its option, the Indemnifying Party may assume the defense of any Third Party Claim by giving written notice to the Indemnified Party within thirty (30) days after the Indemnifying Party's receipt of an Indemnification Claim Notice. Upon assuming the defense of a Third Party Claim, the Indemnifying Party may appoint as lead counsel in the defense of the Third Party Claim any legal counsel selected by the Indemnifying Party (the Indemnifying Party will consult with the Indemnified Party with respect to such counsel and a possible conflict of interest of such counsel retained by the Indemnifying Party). In the event the Indemnifying Party assumes the defense of a Third Party Claim, the Indemnified Party will immediately deliver to the Indemnifying Party all original notices and documents (including court papers) received by the Indemnified Party in connection with the Third Party Claim.

(ii) Right to Participate in Defense. Without limiting Section 9.6(d)(i), any Indemnified Party will be entitled to participate in, but not control, the defense of such Third Party Claim and to employ counsel of its choice for such purpose; *provided, however*, that such employment will be at the Indemnified Party's own cost and expense unless (A) the Indemnifying Party has failed to assume the defense and employ counsel in accordance with Section 9.6(d)(i) (in which case the Indemnified Party will control the defense), or (B) the Indemnified Party has received a written opinion of counsel, reasonably acceptable to the Indemnifying Party, to the effect that the interests of the Indemnified Party and the Indemnifying Party with respect to such Third Party Claim are sufficiently adverse to prohibit the representation by the same counsel of both Parties under applicable Law, ethical rules or equitable principles, in which case the Indemnifying Party will assume one hundred percent (100%) of any such costs and expenses of counsel for the Indemnified Party.

(iii) Settlement. With respect to any Third Party Claims that relate solely to the payment of money damages in connection with a Third Party Claim and that will not (A) result in the Indemnified Party's becoming subject to injunctive or other relief, (B) include any admission or concession of liability or wrongdoing on the part of the Indemnified Party, or (C) otherwise adversely affect the business of the Indemnified Party in any manner, and as to which the Indemnifying Party will have acknowledged in writing the obligation to indemnify the Indemnified Party hereunder, the Indemnifying Party will have the sole right to agree to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss, on such terms as the Indemnifying Party, in its sole discretion, will deem appropriate. With respect to all other Losses in connection with Third Party Claims, where the Indemnifying Party has assumed the defense of the Third Party Claim in accordance with Section 9.6(d)(i), the Indemnifying Party will have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss; *provided,* it obtains the prior written consent of the Indemnified Party (which consent will not be unreasonably withheld, delayed or conditioned). Where the Indemnifying Party has assumed the defense of the Third Party Claim in accordance with Section 9.6(d)(i), the Indemnifying Party will not be liable for any settlement or other disposition of a Loss by an Indemnified Party that is reached without the prior written consent of the Indemnifying Party. Regardless of whether the Indemnifying Party chooses to defend or prosecute any Third Party Claim, no Indemnified Party will admit any liability with respect to or settle, compromise or discharge, any Third Party Claim without the prior written consent of the Indemnifying Party, such consent not to be unreasonably withheld, delayed or conditioned.

(iv) Cooperation. Regardless of whether the Indemnifying Party chooses to defend or prosecute any Third Party Claim, the Indemnified Party will cooperate in the defense or prosecution thereof and will furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith, at the Indemnifying Party's expense. Such cooperation will include access during normal business hours afforded to the Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Third Party Claim, and making Indemnified Parties and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder, and the Indemnifying Party will reimburse the Indemnified Party for all its reasonable out-of-pocket costs and expenses in connection therewith.

(v) Costs and Expenses. Except as provided above in this Section 9.6(d), the costs and expenses, including attorneys' fees and expenses, incurred by the Indemnified Party in connection with any claim will be reimbursed on a Calendar Quarter basis by the Indemnifying Party, without prejudice to the Indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to prompt refund in the event the Indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

9.7 Insurance. Each Party will maintain at its sole cost and expense, an adequate liability insurance or self-insurance program (including product liability insurance) to protect against potential liabilities and risk arising out of activities to be performed under this Agreement, including personal injury, physical injury or property damage arising out of the manufacture, sale, use, distribution or marketing of Licensed Products, and upon such terms (including coverages, deductible limits and self-insured retentions) as are customary in the respective industry of such Party for the activities to be conducted by such Party under this Agreement. The coverage limits set forth herein will not create any limitation on a Party's liability to the other under this Agreement. Upon the request of a Party, the other Party will provide evidence of the insurance coverage required by this Section 9.7.

## ARTICLE 10
## Term and Termination

10.1 Term. This Agreement commenced as of the MOU Effective Date (except where it expressly provides will commence as of the Effective Date) and, unless sooner terminated in accordance with the terms hereof or by mutual written consent of the Parties, will continue on a country-by-country basis, until there are no more Royalty payments owed to Nitto in such country with respect to the Licensed Product (the longest such period of time hereunder, the "**Term**"). Upon expiration of the applicable Royalty Term with respect to the Licensed Product in the applicable country, the license contained in Section 2.1 will become fully paid-up, royalty-free, perpetual and irrevocable with respect to the Licensed Product in such country.

10.2 Termination by Nitto.

(a) Breach. Nitto will have the right to terminate this Agreement in full upon delivery of written notice to Omega in the event of a material breach by Omega of its representations, warranties or obligations under this Agreement, *provided that* such breach has not been cured within sixty (60) days after written notice thereof is given by Nitto to Omega specifying the nature of the alleged breach.

(b) Disputed Breach. If Omega disputes in good faith the existence or materiality of a breach specified in a notice provided in accordance with Section 10.2(a), and Omega provides Nitto notice of such dispute within such sixty (60) day period, then Nitto will not have the right to terminate this Agreement under Section 10.2(a) unless and until it is finally determined, in accordance with Section 11.5 that Omega has materially breached this Agreement and Omega has failed to cure such breach within sixty (60) days following such decision. It is understood and agreed that during the pendency of such dispute, all of the terms and conditions of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder. During the pendency of any such dispute, Omega will pay to Nitto all Milestone Payments and Royalty payments set forth herein that may become due during such period.

10.3 Termination by Omega.

(a) Breach. Omega will have the right to terminate this Agreement in full upon delivery of written notice to Nitto in the event of a material breach by Nitto of its representations, warranties or obligations under this Agreement, *provided that* such breach has not been cured within sixty (60) days after written notice thereof is given by Omega to Nitto specifying the nature of the alleged breach.

(b) Discretionary Termination. Omega, at any time after one (1) year following the MOU Effective Date, will have the right to terminate this Agreement in full at its discretion for any or no reason by delivering written notice to Nitto, such termination to be effective thirty (30) days following the date of such notice.

(c) Termination for Good Faith Reason. During the first year after the MOU Effective Date, this Agreement may be terminated on a country-by-country basis, or in its entirety, in Omega's good faith discretion following consultation with the JSC for the following reasons:

(i) there is no reasonable likelihood that (a) the clinical studies for the Licensed Product will be completed, or (b) the Licensed Product will obtain Marketing Authorization Approval (and pricing/reimbursement, if applicable) from a Regulatory Authority in any Major Market Country;

(ii) efficacy, safety, and/or tolerability of the Licensed Product will not achieve the development criteria, or it is otherwise determined that the that the risk profile of the Licensed Product outweigh its benefits; or

(iii) it is unlikely that the Licensed Product will be commercially viable, including due to technical feasibility (whether in manufacture, clinical development or otherwise), profit potential, strategic value or the competitiveness of the Licensed Product, or the relative intellectual property and development positions of the Licensed Product and competitive third-party products.

10.4 Termination Upon Bankruptcy. If either Party makes an assignment for the benefit of creditors, appoints or suffers appointment of a receiver or trustee over all or substantially all of its property, files a petition or commences a proceeding under any bankruptcy or insolvency act in any state or country or has any such petition or application filed against it which is not discharged within sixty (60) days of the filing thereof, then the other Party may thereafter terminate this Agreement effective immediately upon written notice to such Party. All licenses and rights to licenses granted under or pursuant to this Agreement by one Party (the "**Licensor Party**") to the other Party (the "**Licensee Party**") are, and will otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code (the "**Bankruptcy Code**"), licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code ("Insolvency Legislation"). The Parties agree that Licensee Party, as a licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the Bankruptcy Code. The Parties further agree that that upon commencement of a bankruptcy proceeding by or against Licensor Party under the Bankruptcy Code, Licensee Party will be entitled to a complete duplicate of, or complete access to (as Licensee Party deems appropriate), all such intellectual property and all embodiments of such intellectual property to the extent provided for under the Bankruptcy Code. Such intellectual property and all embodiments of such intellectual property will be promptly delivered to Licensee Party (i) upon any such commencement of a bankruptcy proceeding and upon written request by Licensee Party, unless Licensor Party elects to continue to perform all of its obligations under this Agreement, or (ii) if not delivered under clause (i) of this Section 10.4, upon the rejection of this Agreement by or on behalf of Licensor Party and upon written request by the Licensee Party. Licensor Party (in any capacity, including debtor-in-possession) and its successors and assigns (including any trustee) agrees not to interfere with the exercise by Licensee Party or its Affiliates of its rights and licenses to such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist Licensee Party and its Affiliates in obtaining such intellectual property and such embodiments of intellectual property in the possession or control of Third Parties as reasonably necessary or desirable for Licensee Party to exercise such rights and licenses in accordance with this Agreement. The foregoing provisions are without prejudice to any rights Licensee Party may have arising under the Bankruptcy Code or other applicable law.

10.5 Effects of Termination. Upon termination (but not expiration of the Term pursuant to Section 10.1) of this Agreement for any reason:

(a) Cessation of Rights. Except as otherwise expressly provided herein, all rights and licenses granted by Nitto to Omega in Section 2.1 will terminate.

(b) Sell Off. Notwithstanding the termination of Omega's licenses and other rights under this Agreement, Omega will retain the right to distribute, sell or otherwise dispose of its existing inventory of the Licensed Products, in each case that is intended for distribution, sale or disposition in the Territory, for a period of not more than three (3) months following the date of the effective termination, as though this Agreement had not been terminated, and such distribution, sale or other disposition will not constitute infringement of the Patents or other intellectual property or proprietary rights of Nitto or its Affiliates. Omega's right to distribute, sell or otherwise dispose of its existing inventory of the Licensed

Product pursuant to this Section 10.5(b) will be subject to Omega's continuing obligation to pay Royalties with respect to the Net Sales.

10.6 Survival. In addition to the termination consequences set forth in Section 10.5, the following provisions will survive termination or expiration of this Agreement, as well as any other provision that by its terms or by the context thereof, is intended to survive such termination: Article 1 (to the extent applicable to any other surviving provisions), Article 5, Article 7 (with respect to Joint Patents), Article 8 and Article 11, and Section 2.3(b)(v) (only upon the circumstances set forth therein), last sentence of Section 4.4(c) (with respect to a Royalty Term that has expired), the first sentence of Section 6.1 (with respect to Joint Patents), 6.2, 6.3, 6.4 (with respect to Joint Patents), 6.5 (with respect to Joint Patents), 9.3, 9.4, 9.5, 9.6, the last sentence of Section 10.1, 10.4, 10.5 and this Section 10.6. Termination or expiration of this Agreement will not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination or expiration nor preclude either Party from pursuing all rights and remedies it may have hereunder or at Law or in equity with respect to any breach of this Agreement nor prejudice either Party's right to obtain performance of any obligation. All other rights and obligations will terminate upon termination or expiration of this Agreement.

## ARTICLE 11
## General Provisions

11.1 Cumulative Remedies and Irreparable Harm. All rights and remedies of the Parties hereunder will be cumulative and in addition to all other rights and remedies provided hereunder or available by agreement, at Law or otherwise. Each Party acknowledges and agrees that breach of any of the terms or conditions of this Agreement may cause irreparable harm and damage to the other and that such damage may not be ascertainable in money damages and that as a result thereof the non-breaching Party may be entitled to seek from a court equitable or injunctive relief restraining any breach or future violation of the terms contained herein by the breaching Party without the necessity of proving actual damages or posting bond. Such right to equitable relief is in addition to whatever remedies either Party may be entitled to as a matter of Law or equity, including money damages.

11.2 Relationship of Parties. Nothing in this Agreement is intended or will be deemed to constitute a partnership, agency, employer-employee or joint venture relationship between the Parties. No Party will incur any debts or make any commitments for the other, except to the extent, if at all, specifically provided therein. There are no express or implied Third Party beneficiaries hereunder (except for Omega Indemnitees and Nitto Indemnitees for purposes of Section 9.6, and Omega's Sublicensees for purposes of Section 2.3(b)(v)). For clarity, except as expressly provided in Section 2.2 above, Omega does not grant to Nitto any rights or licenses under this Agreement to any Omega IP, Omega's interest in Joint IP, or any other intellectual property rights of Omega.

11.3 Compliance with Law. Each Party will perform or cause to be performed any and all of its obligations or the exercise of any and all of its rights hereunder in good scientific manner and in compliance with all applicable Law.

11.4 Governing Law. This Agreement will be governed by and construed in accordance with the Laws of the State of Massachusetts, United States of America, without respect to any of its conflicts of laws principles to the contrary, *provided that* any dispute relating to the scope, validity, enforceability or infringement of any Patents will be governed by, and construed and enforced in accordance with, the substantive Laws of the jurisdiction in which such Patents apply.

11.5 Dispute Resolution.

(a) Disputes. Disputes arising under or in connection with this Agreement will be resolved pursuant to this Section 11.5; *provided, however*, that in the event a dispute cannot be resolved without an adjudication of the rights or obligations of a Third Party (other than any Omega Indemnitees or Nitto Indemnitees identified in Section 9.6), the dispute procedures set forth in Sections 11.5(b) and 11.5(c) will be inapplicable as to such dispute.

(b) Dispute Escalation. In the event of a dispute between the Parties, the Parties will first attempt in good faith to resolve such dispute by negotiation and consultation between themselves. In the event that such dispute is not resolved on an informal basis within twenty (20) days, any Party may, by written notice to the other, have such dispute referred to each Executive Officers, who will attempt in good faith to resolve such dispute by negotiation and consultation for a thirty (30) day period following receipt of such written notice.

(c) Dispute Resolution.

(i) Except as otherwise set forth in this Agreement, in the event of any unresolved matter, dispute, or controversy or claim arising out of or relating to this Agreement, or the breach, termination, enforcement, interpretation or validity thereof or which this Agreement expressly provides shall be resolved in accordance with this Section 11.5(c) (each, a "Dispute"), the Parties shall refer the Dispute to the Executive Officers (or designees with similar authority to resolve such Dispute), who shall attempt in good faith to resolve such Dispute. If the Executive Officers cannot resolve such Dispute within thirty (30) days of the matter being referred to them in writing, then such Dispute is to be settled by binding arbitration (each such arbitration, an "Arbitration"). Any dispute about the propriety of commencing the Arbitration or the scope or applicability of the agreement to arbitrate shall be finally settled by Arbitration.

(ii) The set, or legal place, or Arbitration shall be New York, New York, and shall be administered by JAMS in accordance with the JAMS International Arbitration Rules and Procedures, applying its Expedited Procedures pursuant to Article 21 thereunder. The Parties acknowledge that this Agreement evidences a transaction involving interstate commerce. Notwithstanding Section 11.4 with respect to the applicable substantive law, any Arbitration conducted pursuant to the terms of this Agreement shall be governed by the Federal Arbitration Act (9 U.S.C. § 1 *et. seq.*).

(iii) If the alleged damages or amount in dispute (claims and counterclaims inclusive) is less than five million USD ($5,000,000) and the dispute does not concern ownership of Intellectual Property developed under this Agreement, the Parties shall appoint a single arbitrator to be selected by mutual agreement or, if the Parties are unable to agree on an arbitrator within fifteen (15) Business Days after the commencement of Arbitration, the arbitrator shall be appointed by JAMS in accordance with its rules, in each case satisfying the criteria set forth below to the maximum extent possible. If the alleged damages or amount in dispute (claims and counterclaims inclusive) is more than five million USD ($5,000,000) or the dispute concerns ownership of Project IP, the Arbitration shall be conducted by a panel of three (3) arbitrators—each Party shall appoint one (1) arbitrator within ten (10) Business Days after the commencement of Arbitration, and the Parties shall jointly appoint the third arbitrator to be selected by mutual agreement within fifteen (15) Business Days after the commencement of Arbitration. Any arbitrator that is not appointed within the allotted time, shall be appointed by JAMS in accordance with its rules, in each case satisfying the criteria set forth below to the maximum extent possible.

(iv) In all cases, the arbitrator chosen by each Party must be a practicing or retired attorney or judge with no less than ten (10) years of biotechnology industry experience and expertise,

including experience and expertise relating to collaboration and license agreements similar to this Agreement, and the third arbitrator must have no less than fifteen (15) years of such experience and expertise. Under no circumstances shall an arbitrator be a current or former employee, attorney or consultant of either Party or its Affiliates. If the Dispute relates primarily to scientific matters, then the arbitrator should also have relevant scientific expertise, including experience and expertise relating to drug discovery, product development, or commercialization. In all cases, each arbitrator shall be fluent in the English language. An arbitrator shall be deemed to meet these qualifications unless a party objects within fifteen
(15) Business Days after the arbitrator is appointed.

(v) Within twenty (20) days following the later of the date of the last hearing or receipt by the arbitrator(s) of the Parties' written submission, including any post-hearing brief, the arbitrator(s) shall render its award in writing. The award of the arbitrator shall be final and binding on the Parties and the Parties undertake to carry it out without delay.

(vi) The Parties expressly consent to the exclusive jurisdiction of and venue in the United States District Court for the Southern District of New York (and, if such federal court rejects jurisdiction for any reason, then the Parties expressly consent to the jurisdiction of and venue in the state courts of the City of New York, State of New York) solely and specifically for the purposes of confirming, vacating, modifying or correcting the award rendered in any Arbitration. The Parties agree and consent to submit themselves to personal jurisdiction in any such action brought in those courts and hereby waive any right to challenge the jurisdiction of those courts over such action or that those courts are an inconvenient forum for such action. The Parties consent to service of process in any such action by certified mail addressed in accordance with the notice provisions of this Agreement, without prejudice to service of process by any other means authorized by applicable Law.

(vii) The Parties hereby agree that any disputed performance or suspended performance pending during the Arbitration will be completed within a reasonable time period following the award of the arbitrator(s) if the award so orders it.

(viii) Notwithstanding anything in this Agreement to the contrary, a Party may seek a temporary restraining order or a preliminary injunction from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss, or damage on a provisional basis.

(ix) All activities undertaken by the arbitrator(s) will be conducted subject to obligations of confidentiality no less restrictive than those set forth in Article 8. Further, the Parties acknowledge and agree that all information exchanged in connection with the Arbitration proceedings, and the conduct of such proceedings and any information produced thereunder shall be Confidential Information under this Agreement and subject to the provisions of Article 8.

(d) Injunctive Relief. Notwithstanding the dispute resolution procedures set forth in this Section 11.5, in the event of an actual or threatened breach hereunder, the aggrieved Party may seek equitable relief (including restraining orders, specific performance or other injunctive relief) in any court or other forum, without first submitting to any dispute resolution procedures hereunder.

(e) Tolling. The Parties agree that all applicable statutes of limitation and time-based defenses (such as estoppel and laches) will be tolled while the dispute resolution procedures set forth in this Section 11.5 are pending, and the Parties will cooperate in taking all actions reasonably necessary to achieve such a result.

(f) Prevailing Party. The prevailing Party in any suit related to this Agreement will be entitled to recover from the losing Party all out-of-pocket fees, costs and expenses (including those of

attorneys, professionals and accountants and all those arising from appeals and investigations) incurred by the prevailing Party in connection with such arbitration or suit.

11.6 Counterparts; Facsimiles. This Agreement may be executed in one or more counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. Facsimile or PDF execution and delivery of this Agreement by either Party will constitute a legal, valid and binding execution and delivery of this Agreement by such Party.

11.7 Headings. All headings in this Agreement are for convenience only and will not affect the meaning of any provision hereof.

11.8 Waiver of Rule of Construction. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement will be construed against the drafting Party will not apply.

11.9 Interpretation. Whenever any provision of this Agreement uses the term "including" (or "includes"), such term will be deemed to mean "including without limitation" (or "includes without limitation"). "Herein," "hereby," "hereunder," "hereof" and other equivalent words refer to this Agreement as an entirety and not solely to the particular portion of this Agreement in which any such word is used. In this Agreement, the word "or" means "and/or". All definitions set forth herein will be deemed applicable whether the words defined are used herein in the singular or the plural. Unless otherwise provided, all references to Sections and Appendices in this Agreement are to Sections and Appendices of this Agreement. References to any Sections include Sections and subsections that are part of the related Section.

11.10 Binding Effect. This Agreement will inure to the benefit of and be binding upon the Parties, their Affiliates, and their respective lawful successors and assigns.

11.11 Assignment. This Agreement may not be assigned by Nitto, nor may Nitto delegate its obligations or otherwise transfer licenses or other rights created by this Agreement, except as expressly permitted hereunder or otherwise without the prior written consent of Omega, which consent will not be unreasonably withheld, conditioned or delayed; *provided that* Nitto may assign this Agreement without such consent to an Affiliate or to its successor in connection with the sale of all or substantially all of its assets or business or that portion of its business pertaining to the subject matter of this Agreement (whether by merger, consolidation or otherwise); *provided that* such Affiliates or Third Party agree to be bound by this Agreement and the relevant provisions of the MDA. Omega may assign this Agreement in whole or in part to an Affiliate or to any Third Party; *provided that* such Affiliate or Third Party agree to be bound by the applicable terms of this Agreement and the MDA.

11.12 Notices. All notices, requests, demands and other communications required or permitted to be given pursuant to this Agreement will be in writing and will be deemed to have been duly given upon the date of receipt if delivered by hand, email, recognized international overnight courier, or registered or certified mail, return receipt requested, postage prepaid to the following addresses:

if to Omega: Omega Therapeutics, Inc.
20 Acorn Park Drive Cambridge, MA 02140
U.S.A.
Attention: Chief Executive Officer
Email:

With a copy to: Chief Legal Officer

If to Nitto: Nitto Denko Corp.
1-1-2 Shimohozumi
Ibaraki, Osaka 567-8680 Japan
Attention: Head of Division, Nucleic Acid Medicine Business Div.
Email:

With a copy to: Director of Strategy Management Dept., Nucleic Acid Medicine Business Div.
Email: and
Nitto BioPharma, Inc. 10618 Science Center
Drive San Diego, CA 92121 U.S.A.
Attention: Vice President Email:

Either Party may change its designated address by notice to the other Party in the manner provided in this Section 11.12.

11.13 Amendment and Waiver. This Agreement may be amended, supplemented, waived or otherwise modified only by means of a written instrument signed by both Parties; *provided that* any unilateral undertaking or waiver made by one Party in favor of the other will be enforceable if undertaken in a writing signed by the Party to be charged with the undertaking or waiver. No failure or delay in enforcing any right, remedy or provision of this Agreement shall constitute a waiver thereof. Any waiver of any rights to act in a specific instance will relate only to such instance and will not be construed as an agreement to waive any rights in any other instance, whether or not similar.

11.14 Severability. In the event that any provision of this Agreement will, for any reason, be held to be invalid or unenforceable in any respect, such invalidity or unenforceability will not affect any other provision hereof, and the Parties will negotiate in good faith to modify this Agreement to preserve (to the extent possible) their original intent.

11.15 Entire Agreement. This Agreement (including all appendices and exhibits hereto and thereto) and the MDA are the sole agreements with respect to the subject matter hereof and thereof and supersede all other agreements and understandings between the Parties with respect to same. If there is any conflict between this Agreement and the MDA with respect to the Collaboration Target, this Agreement will prevail. For the avoidance of doubt, the Parties hereby acknowledge that any liabilities that have accrued under the MOU are reflected in the terms and conditions of this Agreement. If there is any conflict between this Agreement and the MOU, this Agreement will prevail.

11.16 Force Majeure. Each Party will be excused from the performance of its obligations under this Agreement (other than any obligations to pay amounts due hereunder) to the extent that such

performance is prevented or delayed by force majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse will be continued so long as the condition constituting force majeure continues and the nonperforming Party makes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure will mean conditions beyond the reasonable control of the Parties, including an act of God, war, civil commotion, terrorist act, labor strike or lock-out, pandemic (including the COVID-19 pandemic), epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, and failure of plant or machinery (*provided that* such failure could not have been prevented by the exercise of skill, diligence, and prudence that would be reasonably and ordinarily expected from a skilled and experienced person engaged in the same type of undertaking under the same or similar circumstances).

11.17 Further Assurances. Each Party will take all customary and reasonable actions and do all things reasonably necessary or proper, including under applicable Law, to make effective and further the intents and purposes of the transactions contemplated by this Agreement, including executing any further instruments reasonably requested by the other Party.

**[Remainder of this Page Intentionally Left Blank]**

**WITNESS WHEREOF,** the Parties have caused this Collaboration and License Agreement to be executed by their respective duly authorized officers as of the Effective Date.

**NITTO DENKO CORPORATION**

By: /s/ Yosuke Miki

Name: Yosuke Miki

Title: Senior Executive Vice President & CTO

Date: October 12, 2022

**OMEGA THERAPEUTICS, INC.**

By: /s/ Mahesh Karande
Name: Mahesh Karande
Title: President & CEO

Date: October 7, 2022

,.

**Exhibit 23.1**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in Registration Statement Nos. 333-258365 on Form S-8 and 333-268254 on Form S-3 of our report dated March 1, 2023, relating to the consolidated financial statements of Omega Therapeutics, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2022.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 1, 2023

**Exhibit 31.1**

**CERTIFICATION**

I, Mahesh Karande, certify that:

1. I have reviewed this Annual Report on Form 10-K of Omega Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) [omitted];

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2023

By: /s/ Mahesh Karande

**Mahesh Karande**
**President and Chief Executive Officer**

**Exhibit 31.2**

**CERTIFICATION**

I, Joshua Reed, certify that:

1. I have reviewed this Annual Report on Form 10-K of Omega Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) [omitted];

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2023

By: /s/ Joshua Reed

**Joshua Reed**
**Chief Financial Officer**

**Exhibit 32.1**

**CERTIFICATION PURSUANT TO**
**18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Omega Therapeutics, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Mahesh Karande, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 1, 2023

By: /s/ Mahesh Karande
**Mahesh Karande**
**President and Chief Executive Officer**

**Exhibit 32.2**

**CERTIFICATION PURSUANT TO**
**18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Omega Therapeutics, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Joshua Reed, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 1, 2023

By: /s/ Joshua Reed
**Joshua Reed**
**Chief Financial Officer**