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, 2023

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: 001-36296

Carisma Therapeutics Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**26-2025616**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
3675 Market Street, Suite 200 Philadelphia, PA	**19104**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (267) 491-6422

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

Title of each class	Trading Symbol(s)	Name of exchange on which registered
Common Stock, $0.001 par value per share	**CARM**	**The Nasdaq Stock Market LLC**

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 Section 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, a 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 ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates based on the closing sale price as reported on The Nasdaq Stock Market LLC, as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2023, was $275,726,423.

The registrant had 41,542,534 shares of common stock, $0.001 par value per share, outstanding as of March 15, 2024.

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2023. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties, and other 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 these forward-looking statements. Forward-looking statements in this Annual Report on Form 10-K may include, but are not limited to, statements about:

- the timing and conduct of our pre-clinical studies and clinical trial of CT-0525 for solid tumors that over-express human epidermal growth factor receptor 2, or HER2;
- our plans to conduct discovery and pre-clinical testing of the development of *in vivo* chimeric antigen receptor macrophage and monocyte, or CAR-M, therapeutics for up to twelve oncology targets, as well as multiple other targets and indications in connection with our collaboration with ModernaTX, Inc., or Moderna;
- expenses associated with our Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab;
- our ability to obtain additional financing;
- our ability to replicate in later clinical trials positive results found in pre-clinical studies and early-stage clinical trials of our product candidates;
- our ability to successfully enroll patients in our Phase 1 clinical trial of CT-0525 and complete clinical trials;
- our plans to conduct discovery and pre-clinical testing of other product candidates;
- our ability to realize the anticipated benefits of our research and development programs, strategic partnerships, research and licensing programs and academic and other collaborations;
- the timing of applying for and receiving, and our ability to maintain, marketing approvals from applicable regulatory authorities for our product candidates;
- our ability to obtain and maintain intellectual property protection and regulatory exclusivity for CT-0525 and any other product candidates we are developing or may develop in the future;
- acceptance of CT-0525 and any other product candidates we are developing or may develop, if and when approved, by patients, the medical community and third-party payors;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash and cash equivalents;
- the potential advantages of our product candidates;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization and manufacturing capabilities and strategy;
- the potential impact of public health epidemics or pandemics, including the COVID-19 pandemic, and of global economic developments on our business, operations, strategy and goals;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our competitive position;
- the impact of government laws and regulations;
- political and economic developments; and
- such other matters as discussed on this Annual Report on Form 10-K, including Part I, Item 1A, "Risk Factors."

In some cases, forward-looking statements can be identified by terminology such as "aim," "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "goals," "will," "would," "could," "should," "continue" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those expressed or implied by the forward-looking statements. No forward-looking statement is a promise or a guarantee of future performance.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current

intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to the "Company," "Carisma," "we," "us," and "our" refer to Carisma Therapeutics Inc. (formerly Sesen Bio, Inc.) and its consolidated subsidiaries.

References to "Legacy Carisma" refer to CTx Operations, Inc. (formerly CARISMA Therapeutics Inc.) and references to "Sesen Bio" refer to Sesen Bio, Inc. prior to completion of the business combination on March 7, 2023 in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated as of September 20, 2022, as amended, by and among the Company, Legacy Carisma and Seahawk Merger Sub, Inc., a wholly owned subsidiary of the Company, pursuant to which Seahawk Merger Sub, Inc. merged with and into Legacy Carisma, with Legacy Carisma continuing as a wholly owned subsidiary of the Company and the surviving corporation of the merger, or the Merger.

Pursuant to the Merger Agreement, the Company changed its name from "Sesen Bio, Inc." to "Carisma Therapeutics Inc." Following the completion of the Merger, the business conducted by the Company became primarily the business conducted by Legacy Carisma, which is a biopharmaceutical company dedicated to developing a differentiated and proprietary cell therapy platform focused on engineered macrophages, cells that play a crucial role in both the innate and adaptive immune response.

Part I

Item 1. Business.

Overview

We are a clinical-stage cell therapy company focused on using our proprietary CAR-M cell therapy platform to develop transformative immunotherapies to treat cancer and other serious diseases. We have created a comprehensive cell therapy platform to enable the therapeutic use of engineered macrophages and monocytes, which belong to a subgroup of white blood cells called myeloid cells. Our focus is our proprietary CAR-M cell therapy platform, which redirects macrophages against specific tumor associated antigens and enables targeted anti-tumor immunity by utilizing genetically modified myeloid cells (macrophages and monocytes) to express chimeric antigen receptors, or CARs, enabling these potent innate immune cells to recognize specific tumor associated antigens on the surface of tumor cells.

On March 7, 2023, we completed a business combination in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated as of September 20, 2022, pursuant to which the Merger was consummated. Pursuant to the Merger Agreement, we changed our name from "Sesen Bio, Inc." to "Carisma Therapeutics Inc." Following the completion of the Merger, our business became primarily the business conducted by Legacy Carisma.

In late March 2024, following a strategic review of our operating plan for 2024 and future periods, we approved a revised operating plan intended to balance value creation and expense management with our available cash resources. The objective of our revised operating plan is to focus our clinical development efforts on high potential value programs with meaningful near-term milestones and eliminate non-essential expenses and headcount to extend our cash runway. Under this plan, we intend to focus our *ex vivo* oncology clinical development efforts on our follow-on product candidate CT-0525, a CAR-Monocyte intended to treat solid tumors that over-express HER2.

CT-0525 utilizes a novel approach to CAR-M therapy that engineers patients' monocytes directly, without ex vivo differentiation into macrophages. In November 2023, we received United States Food and Drug Administration, or FDA, clearance of our Investigational New Drug application, or IND, for CT-0525, and we expect to treat the first patient in the second quarter of 2024. We believe that CT-0525 has favorable attributes compared to our initial clinical stage product candidate, CT-0508, and that the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. We will also continue to focus on our *in vivo* mRNA/lipid nanoparticle, or LNP, CAR-M programs in partnership with Moderna.

Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities. We have also elected to pause further development of CT-1119, a mesothelin-targeted CAR-Monocyte, pending additional financing.

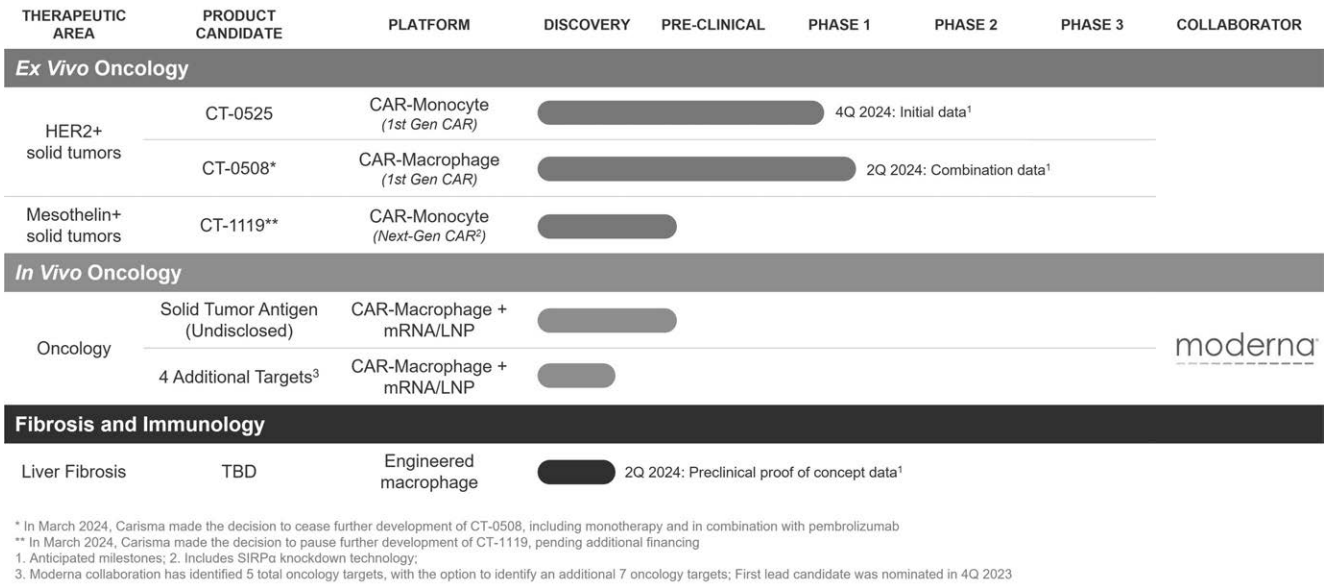
Our early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases, also remains ongoing.

We plan to pursue additional financing and collaboration opportunities to support development of our product candidates and other research and development programs and will continue to re-assess our expense allocation.

Our Product Candidates and Discovery Programs

Using our proprietary macrophage and monocyte cell therapy platform, we are developing a pipeline of product candidates, with an initial focus on advancing multiple *ex vivo* autologous and *in vivo* CAR-M therapies for the treatment of solid tumors. We are also pursuing early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Our *ex vivo* oncology, fibrosis, and

immunology programs are wholly owned. Additionally, under a collaboration agreement with Moderna, we are developing *in vivo* CAR-M therapies utilizing Moderna's mRNA/LNP, technology. Our current pipeline is summarized below:



* In March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab
** In March 2024, Carisma made the decision to pause further development of CT-1119, pending additional financing
1. Anticipated milestones; 2. Includes SIRPα knockdown technology;
3. Moderna collaboration has identified 5 total oncology targets, with the option to identify an additional 7 oncology targets; First lead candidate was nominated in 4Q 2023

Ex Vivo Oncology

CT-0508

Our first product candidate to enter clinical development, CT-0508, is the first CAR-Macrophage to be evaluated in a human clinical trial and is intended to treat solid tumors that over-express HER2, a protein that is over-expressed on the surface of a variety of solid tumors, including breast cancer, gastric cancer, esophageal cancer, salivary gland cancer, and numerous others. CT-0508 has been granted "Fast Track" status for the treatment of patients with HER2 over-expressing solid tumors by the FDA.

CT-0508 is currently being studied in a multi-center open label Phase 1 clinical trial in the United States. This ongoing first-in-human study evaluates the safety, tolerability, and manufacturing feasibility of CT-0508 along with several customary exploratory secondary endpoints. We have completed enrollment of the first group of patients in this trial, with nine patients having been successfully dosed over a five-day dosing schedule. CT-0508 has been generally well tolerated after infusion with no dose-limiting toxicities to date, was successfully manufactured using macrophages obtained from heavily pre-treated, advanced solid tumor patients and has shown high CAR expression, viability, and purity. In addition to the first group of patients in this study, we initiated a second group to evaluate bolus dosing of patients and we presented data from five patients in the second group in the third quarter of 2023. While the results from this early clinical trial data are both preliminary and limited, we believe the combined group 1 and group 2 results support the preliminary results from this trial indicating that CT-0508 can potentially be detected within the tumor microenvironment, or TME, and induce anti-tumor adaptive immunity. In group 1, a best overall response, or BOR, of stable disease was seen in 4 out of 9 patients, and in group 2, the BOR was progressive disease. Translational analyses combining group 1 and group 2 demonstrated a correlation between TME activation, T cell activation, and HER2 status with BOR of stable disease.

Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities.

CT-0508 and Pembrolizumab Combination Sub-Study

We have initiated a sub-study evaluating the co-administration of CT-0508 and pembrolizumab, a programmed cell death protein 1, or PD-1 checkpoint inhibitor, in the clinical setting. We have observed synergistic potential of CT-0508 with a PD-1 checkpoint inhibitor in multiple pre-clinical models. As a result of those studies and the preliminary results from

group 1 in our monotherapy treatment clinical trial discussed above, we initiated a sub-study in the first quarter of 2023 to evaluate patients with the co-administration of CT-0508 and pembrolizumab. We have enrolled six patients in the sub-study. We expect to report data from this sub-study in the second quarter of 2024.

Although we plan to continue ongoing activities under our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities.

We also initiated several other sub-studies evaluating CT-0508 in the clinical setting, as further described below. However, these sub-studies have been placed on hold as part of our recently announced revised operating plan and we do not intend to enroll patient in these sub-studies.

CT-0525

Our follow-on product candidate, CT-0525, a CAR-Monocyte intended to treat solid tumors that over-express HER2, utilizes a novel approach to CAR-M therapy. The patient's monocytes are engineered *ex vivo* without being differentiated into macrophages, as we currently do for CT-0508. The CAR-Monocyte approach utilizes a single day manufacturing process, which enables the manufacture of up to ten billion cells from a single apheresis. Apheresis is a medical technology in which the blood of the patient is passed through an apparatus that separates out the white blood cells and returns the remainder of the blood to the circulation. The manufacturing approach for CAR-Monocytes leverages an automated, closed-system manufacturing process. In addition, the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. By increasing the cell yield, a CAR-Monocyte enables a larger dose than a CAR-Macrophage. In addition, a CAR-Monocyte has the potential for improved persistence and trafficking, which were observed in pre-clinical studies. We believe that the increased cell yield and the improved persistence and trafficking may improve tumor control. In November 2023, we received FDA clearance of our IND for CT-0525 and we expect to treat the first patient in the second quarter of 2024. Based on our recently announced revised operating plan, we intend to focus our *ex vivo* oncology clinical development efforts on CT-0525.

CT-1119

Our pipeline also includes additional tumor targets, encompassing diverse solid tumor indications with significant unmet medical needs. CT-1119 is a mesothelin-targeted CAR-Monocyte that is designed to treat patients with advanced mesothelin-positive solid tumors, including lung cancer, mesothelioma, pancreatic cancer, ovarian cancer, and others. CT-1119 incorporates two key enhancements: (1) a next-generation CAR that, in pre-clinical studies, led to a significant increase in tumor killing and cytokine release, and (2) the incorporation of a signal-regulatory protein alpha, or SIRPα, knockdown to overcome the cluster of differentiation, or CD,47 immune checkpoint. We have elected to pause further development of CT-1119 as part of our revised operating plan, pending additional financing.

In Vivo Oncology

In addition to the development of *ex vivo* CAR-M cell therapies, we are developing *in vivo* CAR-M cell therapies, wherein immune cells are directly engineered within the patient’s body. To advance our *in vivo* CAR-M therapeutics, we established a strategic collaboration with Moderna. In the fourth quarter of 2023, we presented pre-clinical data from this collaboration demonstrating that CAR-M can be directly produced *in vivo*, successfully redirecting endogenous myeloid cells against tumor-associated antigens using mRNA/LNP. Additionally, the pre-clinical data demonstrated feasibility, tolerability, and early efficacy of *in vivo* CAR-M against metastatic solid tumors. In December 2023, we announced the nomination of the collaboration's first lead candidate, which will target an antigen present on a solid tumor with significant unmet medical need.

Fibrosis and Immunology

In addition to acting as a first line of defense in the innate immune system, macrophages and monocytes are found in all tissues in the body where they serve key regulatory functions such as wound healing, termination of immune responses and tissue regeneration. Using our macrophage and monocyte engineering platform, we are pursuing early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Pre-clinical proof of concept for fibrosis is targeted for the second quarter of 2024.

Our Strategy

Our goal is to build upon our leadership position in bringing macrophage- and monocyte-based cell therapies to patients with cancer and other serious diseases. To achieve our vision, we have developed our proprietary CAR-M cell therapy platform, a pipeline of assets spanning numerous indications with unmet medical needs, a robust discovery engine, broad intellectual property, robust manufacturing capabilities, and a dedicated executive team with extensive experience in cell therapy and drug development, manufacturing, and commercialization and leading scientific expertise in the field.

We intend to prioritize our clinical development efforts on high potential value programs with meaningful near-term milestones while managing our expense allocation.

The key pillars of our strategy include:

- **Leverage Leadership in Macrophage- and Monocyte-Based Cell Therapies:** Despite the incredible promise shown by cell therapies for hematologic malignancies, the success has not been replicated in the solid tumor setting. Macrophage and monocyte cell therapies hold promise in addressing the limitations of other cell types and transforming the cell therapy treatment paradigm for solid tumors. The inherent biology of macrophages and monocytes offers several potential advantages that directly apply to current barriers for cell therapy efficacy in the solid tumor context. Our proprietary CAR-M platform is designed to enable the therapeutic use of engineered macrophages and monocytes for the treatment of cancer and other serious diseases and disorders. The CAR-M platform incorporates proprietary tumor targeting constructs, vectors to deliver CARs to macrophages and monocytes and novel manufacturing processes. Beyond our CAR-M technologies, we are pursuing multiple platform enhancements for our CAR constructs, editing technologies, and therapeutic delivery vehicles including gene edited induced pluripotent stem cells, or iPSC-derived, macrophages and mRNA-based *in vivo* CAR-M.

- **Advance our HER2 program:** Our anti-HER2 clinical candidate CT-0525 is an *ex vivo* autologous cell therapy product candidate, wherein immune cells from blood drawn from a patient are engineered outside of the body and reinfused into the same patient. We are focused on advancing CT-0525 with a goal of identifying the Phase 2/3 regimen for the product candidate in 2025. We believe that CT-0525 has favorable attributes compared to CT-0508, and that the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage.

- **Progress Pre-Clinical Oncology Pipeline:** Beyond the HER2 program, we plan to advance additional pipeline candidates targeting diverse solid tumor indications with substantial unmet medical needs. For example, we have a broad strategic collaboration with Moderna focused on the development of *in vivo* CAR-M therapeutics for up to 12 oncology targets, of which five have already been nominated. The first lead candidate nominated, announced in December 2023, will target an antigen present on a solid tumor with a significant unmet medical need.

- **Diversify Beyond Oncology:** Leveraging our macrophage and monocyte engineering platform, we are pursuing early research and development opportunities for treating diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Pre-clinical proof of concept in fibrosis utilizing our engineered platform is expected in the second quarter of 2024.

- **Forge Strategic Partnerships:** Given the breadth of opportunities enabled by the macrophage and monocyte engineering platform, we may opportunistically enter into strategic partnerships or collaborations to maximize the potential of our platform.

These strategic imperatives collectively position us at the forefront of advancing macrophage- and monocyte-based cell therapies, with a commitment to innovation, clinical progress, and a diversified approach beyond oncology.

Background

Limitations of Current CAR-T or CAR-NK Therapies

Cellular immunotherapy is a type of immuno-oncology approach whereby human immune cells are utilized to recognize and destroy cancer cells in a targeted manner.

Despite the incredible promise shown by cell therapies for hematologic malignancies, the success has not been replicated in the solid tumor setting. There are numerous challenges impacting T and NK cell immunotherapy in patients with solid

tumors, such as the inability of cells to appropriately access the TME, overcome immunosuppression in the TME, and overcome target antigen heterogeneity. Importantly, there have been challenges in targeting solid tumors with CAR-T cells without inducing toxicities against normal tissues or inducing severe systemic cytokine release syndrome, or CRS. To date, no CAR therapies for the treatment of solid tumors have received marketing approval.

The Opportunity for Engineered Macrophages in Treating Cancer

We believe that macrophage and monocyte cell therapies hold promise in addressing the limitations of other cell types and transforming the cell therapy treatment paradigm for solid tumors and other immunologic and inflammatory diseases. The inherent biology of macrophages and monocytes offers several potential advantages that directly apply to current barriers for cell therapy efficacy in the solid tumor context.

Macrophages and monocytes are actively recruited into solid tumors, while other immune cells, such as T cells, are often actively excluded. Macrophages are professional phagocytic cells capable of directly killing tumor cells through this unique mechanism. In addition to direct killing, macrophages can secrete pro-inflammatory factors that convert the immunosuppressive TME into an environment that promotes immunity. Importantly, macrophages and monocytes are professional antigen presenting cells, meaning they can directly present tumor-derived antigens to T cells leading to anti-tumor T cell responses, a phenomenon known as epitope spreading. Epitope spreading enables activity against tumor cells which either lack or lose expression of the initial antigen targeted by the CAR — a key challenge for cell therapies — and ultimately enables macrophages and monocytes to overcome target antigen heterogeneity within the patient's cancer.

In addition to acting as a first line of defense in the innate immune system, macrophages and monocytes are found in all tissues in the body where they serve key regulatory functions such as wound healing, termination of immune responses and tissue regeneration. The prevalence and diversity of function of macrophages and monocytes make them an attractive potential therapeutic delivery cell.

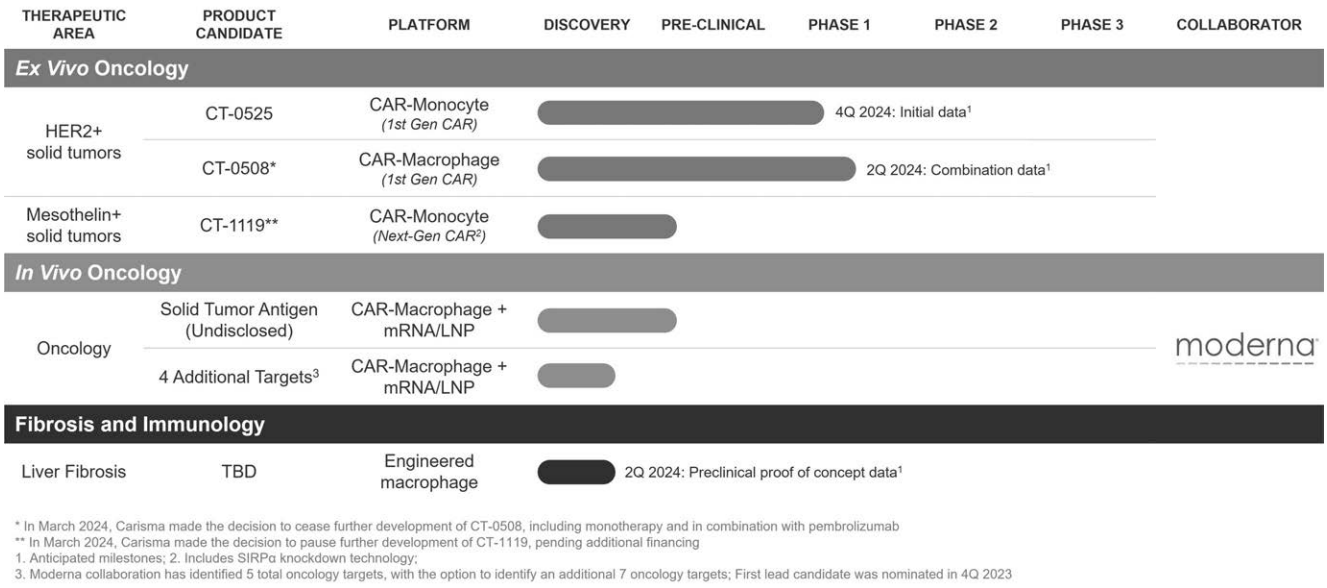
We believe an approach which harnesses the direct effector functions of macrophages or monocytes, optimizes their activation status toward an inflammatory phenotype, and redirects phagocytosis with molecular specificity would represent a major advance in cancer immunotherapy and other serious diseases.

CAR-M Pre-clinical data

CAR-M have the potential to address the key challenges involved in treating solid tumors. Pre-clinical studies with CAR-M have demonstrated the ability to infiltrate solid tumors, phagocytose and destroy tumor cells directly, and present tumor-derived antigens leading to activation of the adaptive immune system. CAR-M mount anti-tumor immunity in numerous ways. First, CAR-M leverage the natural tumor-homing ability of macrophages and monocytes, the naturally most abundant immune cells in the TME, to traffic to both primary tumors and metastases, enabling engineered macrophages to act as a "Trojan horse," tricking the tumor into recruiting engineered, anti-tumor CAR-M as if they were normal monocytes or macrophages. Once within the tumor, CAR-M directly kill antigen-expressing tumor cells through phagocytosis and secretion of cytotoxic factors. CAR-M secrete inflammatory cytokines and chemokines that promote a pro-inflammatory environment and lead to the recruitment of T cells and other leukocytes. Finally, CAR-M serve as professional antigen presenting cells for T cells, inducing epitope spreading, systemic anti-tumor immunity, and immune memory against tumor antigens, expanding anti-tumor immunity to target negative tumor cells and potentially preventing antigen negative relapse.

Pipeline of Product Candidates and Discovery Programs

Using our proprietary CAR-M platform, we are developing a broad pipeline of product candidates, with an initial focus in oncology.



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***Ex Vivo* Oncology**

Rationale for CAR-M Therapy for HER2+ Solid Tumors

While therapies targeting solid tumors that over-express HER2 have led to improved survival rates in breast, gastric and gastro-esophageal junction cancers, there remains an unmet need in patients with advanced HER2 over-expressing cancers, including metastatic lung, ovarian, colon, bladder, and other cancers, which have exhausted all approved therapies including the approved anti-HER2 therapies.

Approximately 20% of breast cancers over-express HER2, a protein that is over-expressed on the surface of a variety of solid tumors. In addition to breast, gastric, and gastroesophageal junction cancers, HER2 is also over-expressed in a number of solid tumor indications including but not limited to bladder cancer, ovarian cancer, lung cancer and colon cancer.

HER2 has several advantages as a target antigen for CAR-M. In addition to being over-expressed in a variety of solid tumor types with significant unmet medical need, HER2 is not shed or internalized, and it is expressed at low levels in non-tumor tissues. As HER2 expression is typically maintained over the course of disease, CAR-M may be developed for treatment of metastatic disease, for example, in the liver and lung, as well as primary tumors. Additionally, HER2 is typically not lost after patients with metastatic cancer progress on available HER2 targeted therapies, rendering HER2 refractory patients potentially eligible for CAR-M therapy.

First Product Candidate: CT-0508 (anti-HER2 CAR-Macrophage)

CT-0508 is a cell product comprised of autologous, peripheral blood monocyte-derived, pro inflammatory macrophages, transduced with a chimeric adenoviral vector, Ad5f35, containing an anti-HER2 CAR. HER2 is a protein on the cell surface that promotes the growth of cancer cells. The anti-HER2 CAR is a first-generation CAR composed of a fully human single-chain variable fragment, or scFv, derived from the monoclonal antibody, or mAb, trastuzumab, which is specific for human HER2. The anti-HER2 scFv is fused to a CAR backbone containing a CD8 hinge, CD8 transmembrane domain, and a CD3ζ intracellular domain. The CAR is cloned into an adenoviral vector backbone and transduced into monocyte-derived macrophages. Based on the pre-clinical data generated to date, CT-0508 CAR-Macrophages are able to specifically recognize HER2 over-expressing tumor cells, which triggers both direct killing of tumor cells and phagocytosis. Additionally, CAR engagement to HER2 on tumor cells results in the secretion of a broad array of pro-

inflammatory cytokines and chemokines, which contribute to the recruitment and activation of additional immune cells to the TME, including effector T cells and other antigen presenting cells. CT-0508 CAR-Macrophages are antigen presenting cells, and after phagocytosing tumor cells they process tumor-derived antigens and present them to T cells, leading to T cell immunity against tumor antigens. This additional activation of the adaptive immune system amplifies anti-tumor immune response and can lead to long term immune memory not only against HER2, the primary target, but other tumor specific neoantigens as well.

CT-0508 is currently being studied in a multi-center open label Phase 1 clinical trial in the United States. As of the date of this Annual Report on Form 10-K, seven clinical sites are open for screening and enrollment: (i) the University of Pennsylvania Abramson Cancer Center, (ii) the University of North Carolina Lineberger Comprehensive Cancer Center, (iii) the City of Hope National Medical Center, (iv) the MD Anderson Cancer Center, (v) the Sarah Cannon Cancer Research Institute, (vi) Oregon Health and Science University, and (vii) the Fred Hutchinson Cancer Center. The FDA has granted "Fast Track" status to CT-0508 for the treatment of patients with HER2 over-expressing solid tumors.

Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities.

CT-0508 Clinical Data — Study 101

The ongoing first-in-human Phase 1 study primarily evaluates the safety, tolerability and manufacturing feasibility of CT-0508 along with several customary exploratory secondary endpoints. We have completed enrollment of the first group of patients in this trial, with nine patients having been successfully dosed over a five-day dosing schedule. CT-0508 has been generally well tolerated after infusion with no dose-limiting toxicities to date, was successfully manufactured using macrophages obtained from heavily pre-treated, advanced solid tumor patients and has shown high CAR expression, viability, and purity. In addition to the first group of patients in this study, we initiated a second group to evaluate bolus dosing of patients and we presented data from five patients in the second group in the third quarter of 2023. While the results from this early clinical trial data are both preliminary and limited, we believe the combined group 1 and group 2 results support the previously presented preliminary results from this trial indicating that CT-0508 can potentially be detected within the TME and induce anti-tumor adaptive immunity. We have also initiated several sub-studies evaluating CT-0508 in the clinical setting. In addition to monotherapy treatment, we have observed synergistic potential of CT-0508 with a PD-1 checkpoint inhibitor in multiple pre-clinical models. As a result of those studies and the preliminary results from group 1 in our clinical trial, we initiated a sub-study in the first quarter of 2021 to evaluate patients with the co-administration of CT-0508 and pembrolizumab, a PD-1 checkpoint inhibitor. We have enrolled six patients in the sub-study. We anticipate reporting data from this sub-study in the second quarter of 2024.

Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities.

Additional CT-0508 Sub-Studies

CT-0508 Intraperitoneal administration sub-study

This sub-study has been designed to assess the safety and feasibility of CT-0508 via regional administration into the peritoneal cavity. The target population for this sub-study are subjects at least 18 years of age who meet inclusion criteria per the main protocol, that have HER2 over-expressing gynecological cancers including but not limited to ovarian, fallopian tube, primary peritoneal, and endometrial cancers, who have disease spread mainly within the peritoneal cavity that meet the sub-study specific eligibility criteria. We have elected to place this sub-study on hold for expense reduction purposes.

CT-0508 Biodistribution sub-study

This open-label sub-study is designed to evaluate the whole body biodistribution of CT-0508 after intravenous administration using radiolabeled CT-0508 and longitudinal positron emission tomography and computed tomography, or PET/CT, imaging. This sub-study includes ^{89}Zr-oxine radiolabeling a fraction of the CT-0508 cell product, followed by administration on Day 1 and PET/CT imaging approximately on Day 1, 4, 8, 15, and 28 to assess trafficking and

biodistribution of CT-0508. The target population for this sub-study are subjects at least 18 years of age that meet inclusion criteria per the main protocol. We have elected to place this sub-study on hold for expense reduction purposes.

CT-0525 (anti-HER2 CAR-Monocyte)

Our follow-on product candidate, CT-0525, a CAR-Monocyte, is a cell product comprised of autologous, peripheral blood monocytes, transduced *ex vivo* with a chimeric adenoviral vector, Ad5f35, containing an anti-HER2 CAR. CT-0525 is in clinical development and utilizes a novel *ex vivo* approach to CAR-M therapy that engineers patients' monocytes directly, without differentiation into macrophages, as we currently do for CT-0508. CT-0525 will be administered to patients, wherein it will traffic to and enter tumor tissue, differentiating into macrophages *in vivo* rather than *ex vivo*. The novel CAR-Monocyte approach enables a single day manufacturing process, enables the ability to manufacture up to ten billion cells from a single apheresis, and leverages an automated, closed-system manufacturing process. By increasing the cell yield, the CAR-Monocyte approach enables a larger dose than with CAR-Macrophages. In addition, CAR-Monocytes have the potential for improved persistence and trafficking, which were observed in pre-clinical studies. The increased cell yield and the improved persistence and trafficking may improve tumor control. In November 2023, we received FDA clearance of our IND for CT-0525 and we expect to treat the first patient in the second quarter of 2024.

CT-0525 Clinical Study Design — Study 102

CT-0525 is currently being studied in a multi-center open label Phase 1 clinical trial in the United States. The Phase 1 clinical trial for CT-0525 is a single-arm, open-label study of systemic intravenous administration of CT-0525. This study is intended to evaluate safety, tolerability, and the manufacturing feasibility of CT-0525. Secondary endpoints will also be evaluated including cellular kinetics, overall response rate, or ORR, and duration of response, or DOR. This study will enroll participants with locally advanced (unresectable) or metastatic solid tumors over-expressing HER2 whose disease has progressed on standard approved therapies. The study will consist of two cohorts: Cohort 1 will receive IV administration of three billion CAR-positive cells, while Cohort 2 will receive IV administration of up to 10 billion CAR-positive cells. In late March 2024, we determined to focus clinical development primarily on CT-0525, as we believe that CT-0525 has favorable attributes compared to CT-0508, and that the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage.

CT-0525: Pre-clinical Development

In pre-clinical studies, CT-0525 was successfully generated with high cell yield, CAR expression, viability, and purity in a rapid, one day manufacturing process. The manufacturing process enabled the production of $10x10^9$ (ten billion) cells, approximately 5-fold higher than the cell number produced in the CT-0508 process. *In vivo*, CT-0525 demonstrated significantly enhanced persistence with a half-life of 45 days – an approximately 10-fold increase compared to CT-0508. CT-0525 tumor trafficking was significantly enhanced compared to CT-0508, demonstrating an approximately 40-fold increase in tumor accumulation at early time points. Taken together, the increased dose, trafficking potential, and persistence yields an expected 2,000-fold increased total exposure compared to CT-0508. Mechanistically, CT-0525 differentiated into CAR-Macrophages efficiently and adopted the appropriate inflammatory (M1) phenotype and resisted conversion to undesirable phenotypes in immunosuppressive environments, which may be found in tumors. CT-0525 was able to kill tumors cells as early as two days post transduction and showed enhanced killing as fully differentiated macrophages, seven days post transduction. CT-0525 released a variety of pro-inflammatory cytokines and chemokines that have the potential to activate T cells and induce an anti-tumor immune response. CT-0525 controlled tumor growth in multiple *in vivo* solid tumor models. We believe that CAR-Monocytes represent a potentially promising approach for cancer immunotherapy, with the potential for increased dose, tumor infiltration, persistence, and potency compared to the CAR-Macrophage CT-0508.

CT-1119 (Anti-Mesothelin CAR-Monocyte)

CT-1119 is a mesothelin-targeted CAR-Monocyte developed for study in patients with advanced mesothelin-positive solid tumors, including lung cancer, mesothelioma, pancreatic cancer, ovarian cancer, and others. We have selected a clinical candidate for CT-1119, which will incorporate two key enhancements: (i) a next-generation CAR that, as demonstrated in pre-clinical studies, leads to a significant increase in tumor killing and cytokine release, and (ii) the incorporation of SIRPα knockdown to overcome the CD47 immune checkpoint.

Mesothelin is a well validated tumor associated antigen. Mesothelin has been shown to be aberrantly expressed on the surface of tumor cells and plays an important role in promoting cancer invasion and proliferation. Mesothelin has been demonstrated to be expressed at high levels in mesothelioma, lung cancer, ovarian cancer, pancreatic cancer, and other

solid tumors with limited expression in normal tissue. Mesothelin positive solid tumors represent a significant unmet medical need.

We have elected to pause further development of CT-1119, pending additional financing.

Next-Gen CAR Design

We are developing additional next generation CAR-M improvements utilizing enhanced CAR constructs to increase potency and functionality of the engineered cells. This includes optimization of each element of the CAR itself — the binder (which gives the CAR specificity to a target antigen), the hinge (which connects the binder to the transmembrane domain and gives the CAR length and flexibility), the transmembrane domain (which spans the cell membrane), and the intracellular signaling domains (which are responsible for activation of immune cell function). These changes can lead to increased proinflammatory cytokine release and more potent *in vitro* and *in vivo* killing relative to the first-generation CAR construct.

SIRPα Knockdown

We have also developed gene editing technologies for enhancing anti-tumor CAR-M functions. Macrophages naturally express the inhibitory receptor SIRPα, which suppresses phagocytosis after stimulation with CD47. Solid tumors can over-express CD47 to evade phagocytosis by macrophages. We have previously demonstrated using CRISPR/Cas9 that SIRPα knockout, or KO, can enhance CAR-M killing and phagocytosis of tumor cells.

We have now developed a proprietary single-vector system to simultaneously deliver CAR and targeted gene knockdown. A novel vector was designed to introduce custom shRNA into a synthetic CAR intron under a shared promoter. Expression of this vector concomitantly produces CAR mRNA and SIRPα-targeting shRNA.

We demonstrated that the intronic shRNA vector could deliver HER2-targeting CAR, reduce SIRPα expression, and enhance anti-tumor functions of primary human CAR-M. Importantly, the one-step vector design was as proficient as transduction followed by CRISPR/Cas9 editing. We also demonstrated that the intronic shRNA vector improved tumor clearance *in vivo*, as compared to unedited CAR-M.

The intronic shRNA design is a generalizable technology that is valuable for additional CAR designs, target tumor antigens, and gene knockdown targets. The modular adenoviral vector introduces gene editing capabilities while remaining compatible with pre-existing manufacturing strategies. We have incorporated our proprietary intronic shRNA vector into the CT-1119 platform to enhance anti-tumor functions and overcome the CD47 checkpoint.

Synergistic Potential of CAR-M Therapy with T cell Checkpoint Inhibitors

Blocking the immune checkpoint molecule PD-1 checkpoint inhibitor, has revolutionized cancer treatment for patients with a multitude of solid tumor indications. Pembrolizumab is a potent humanized immunoglobulin G4, or IgG4, mAb, with high specificity of binding to the PD-1 checkpoint inhibitor receptor, inhibiting its interaction with programmed cell death ligand 1, or PD-L1, and programmed cell death ligand 2, or PD-L2. While pembrolizumab is currently indicated for the treatment of patients across several solid tumor indications, the majority of patients have either primary or secondary resistance to immune checkpoint blockade and may benefit from combinatorial therapy that could overcome immune cell exclusion, poor antigen presentation, low T cell infiltration, high tumor-associated macrophages, or TAM, infiltration, a lack of productive co-stimulation, low mutational burden, intra-tumoral, or IT, immunosuppression, and a low frequency of tumor reactive T cell clones.

Based on the data generated during pre-clinical development, CT-0508 is able to specifically recognize cancer cells through the binding of the CAR to HER2 expressed on the surface of the cancer cells. This interaction triggers activation of the CAR-M and results in direct anti-tumor effect by killing and phagocytosis of the tumor cells. In addition, CT-0508 recruits T cells, activates the TME, and as professional antigen presenting cells, can process and present tumor associated antigen and/or neoantigens expressed by the tumor cells, leading to T cell immunity against these specific antigens. However, this indirect anti-tumor effect involves the engagement of T cells that may be actively suppressed, or exhausted, within the TME by a variety of factors including secreted immune-modulatory factors and inhibitory ligands expressed on both immune and tumor cells. Additionally, several studies have demonstrated that patients with low mutational burden, low major histocompatibility complex expression, defective antigen presentation, low CD8+ T cell infiltration, or minimal

Type 1 T helper, or Th1, cytokine signatures tend to be unresponsive to PD-1 checkpoint inhibitor blockade. Therefore, based on the mechanism of action of CT-0508 and the limitations of PD-1 checkpoint inhibitor blockade, the combination of CAR-M therapy with PD-1 checkpoint inhibitor blockade therapy may be beneficial as CT-0508 will drive TME remodeling and enhance antigen presentation (innate immunity) to initiate an anti-tumor T cell response (adaptive immunity) which will be strengthened by inhibiting the PD-1 checkpoint inhibitor pathway.

CT-0508 and pembrolizumab combination sub-study design

This open-label sub-study assesses the safety and tolerability of co-administering CT-0508 in combination with the PD-1 checkpoint inhibitor, pembrolizumab. The target population for this sub-study are subjects who have HER2 over-expressing solid tumors and meet the eligibility criteria. The sub-study was initiated in the first quarter of 2023 and enrolled six patients with the co-administration of CT-0508 and pembrolizumab. We anticipate reporting data for this sub-study in the second quarter of 2024. Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities.

***In Vivo* Oncology**

mRNA/LNP Platform

In collaboration with Moderna, we are developing an mRNA based *in vivo* CAR-M platform for oncology. This approach is highly differentiated in the cell therapy space — not only because it relies on myeloid cells as the engineered effectors, but also because it utilizes direct *in vivo* reprogramming of patients' own cells with a well-validated mRNA/LNP platform. By engineering patients' own cells directly within their body, *ex vivo* autologous or allogeneic cell manufacturing is entirely bypassed. Importantly, while this approach enables an off-the-shelf therapy, the engineered cells are autologous, as it is the patients' own cells being engineered into CAR-M *in vivo*, or directly within their body. This strategic partnership enables us to apply the learnings gleaned from autologous CAR-M development to expand our pipeline to up to 12 additional oncology candidates, of which five have already been identified as research targets.

Studies with the LNP have shown mRNA delivery leads to CAR expression on myeloid cells (monocytes, macrophages, and dendritic cells). Based on clinical data using other (non-CAR) payloads, Moderna has previously demonstrated that the LNP was well-tolerated after systemic administration and could also be re-dosed. Preliminary data have demonstrated that the LNP is efficient in transfecting myeloid cells *in vitro* and *in vivo*. In addition, preliminary data confirms high CAR expression, viability, and CAR-M function. In the fourth quarter of 2023, we presented pre-clinical data from this collaboration demonstrating that CAR-M can be directly produced *in vivo*, successfully redirecting endogenous myeloid cells against tumor-associated antigens using mRNA/LNP. Additionally, the data demonstrated feasibility, tolerability and early efficacy of in vivo CAR-M against metastatic solid tumors. In December 2023, we announced nomination of the collaboration's first lead candidate, which will target an antigen present on a solid tumor with significant unmet medical need.

Fibrosis and Immunology

Fibrosis

While we are an oncology focused company, our macrophage and monocyte cell engineering platform offers broad opportunity to develop cell therapies for indications beyond oncology. We have numerous early-stage research programs designed to produce development candidates for liver fibrosis and other immunologic and inflammatory diseases. Our new product candidates will incorporate all the core elements of our macrophage and monocyte cell engineering platform, plus certain indication specific modifications uniquely designed to address the pathology of each indication. While autologous cell therapy may be utilized for proof of concept, these indications have the potential to be combined with our allogeneic or off-the-shelf therapeutic approaches. Pre-clinical proof of concept in fibrosis is expected in the second quarter of 2024.

Manufacturing and Delivery

We do not own or operate, and currently have no plans to establish, our own manufacturing facilities. We currently rely on and expect to continue to rely on third-party contract manufacturing organizations, or CMOs, for the manufacturing and

release testing of viral vectors and cell drug products. We also currently rely on third parties for patient leukapheresis material logistics as well as to package, label, store, and distribute the cell drug products.

We have established and will continue to establish arrangements with contract manufacturers to supply clinical materials and manufacturing capabilities for our clinical trials. We currently obtain our supplies from these manufacturers on a purchase order basis and does not have long-term supply arrangements in place. Should any of these manufacturers become unavailable to us for any reason, we believe that there are several potential replacements, although we may incur some delay in identifying and qualifying such replacements.

We also plan to continue to expand the scope and number of our collaborations to further develop our manufacturing capabilities and to minimize manufacturing risk. As we scale to commercialization, we expect to increase our capacity with our current suppliers and evaluate other options to secure commercial scale capacity.

Manufacturing Process for CT-0525

A CMO is used to produce viral vector. The CT-0525 drug substance process begins by isolating the monocyte population from a fresh patient leukopak mobilized by donor pretreatment with filgrastim. The resulting monocytes are then transduced in media containing a cytokine and the Ad5f35 vector encoding an anti-HER2 CAR. The resulting drug substance cells are continuously processed, formulated, and transferred into freezing bags to generate drug product. Monocytes from one patient's leukopak comprise one batch of CT-0525. The drug product is carefully frozen in a controlled process and then placed into secured storage and maintained at a temperature of <-135 ºC. Safety and specification tests are performed and if found acceptable the product is released and shipped to clinical trial sites. The current process from receipt of leukopak to drug product and cryopreservation is one day.

Manufacturing Process for CT-0508

A CMO is used to produce viral vector. The CT-0508 drug substance process begins by isolating the monocyte population from a single fresh patient leukopak mobilized by donor pretreatment with filgrastim. The resulting monocytes are cultured in the presence of a cytokine and other factors to induce differentiation into macrophages. The resulting macrophages are then transduced with the Ad5f35 vector encoding an anti-HER2 CAR. The resulting cells are then harvested as drug substance. Macrophages derived from a single leukopak from one patient comprise one batch of CT- 0508. Final formulation is performed and transferred into freezing bags to generate drug product. The drug product is carefully frozen in a controlled process and then placed into secured storage and maintained at a temperature of <-135 ºC. Safety and specification tests are performed and if found acceptable the product is released and shipped to clinical trial sites. The current process from receipt of leukopak to drug product and cryopreservation is eight days. We plan to continue to invest in process improvements to reduce the overall manufacturing process time and improve costs for the viral vector and cell drug.

Intellectual Property

We strive to protect and enhance our proprietary technology, inventions and improvements that we believe are commercially important to the development of our business, including through seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also intend to rely on trade secrets related to our proprietary technology platform and our know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the fields of cancer and other indications including those related to fibrosis and other immunologic and inflammatory diseases, which may be important for the development of our business. We also may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available.

Our commercial success may depend, in part, on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend, and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. With respect to both our owned and licensed intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we file in the

future, nor can we be sure that any of our existing patents or any patents that may be granted us in the future will be commercially useful in protecting our commercial products and methods of manufacturing such products, as well as being held valid if challenged.

We currently control over 26 granted patents, which are expected to expire at various times between 2033 and 2042, and over 104 patent applications pending in several jurisdictions, including the United States, Europe, Australia, Brazil, Canada, China, Israel, Japan, Korea, Mexico, New Zealand, and Singapore. Intellectual property is a critical component of our business plan for maximizing return on our investments. We are actively developing intellectual property and will continue to maintain and defend United States and international patent rights for our products, technology, and development and improvement of our discovery platforms.

To maintain our competitive position in the market, we have spent considerable effort and resources securing intellectual property rights, including several patent rights related to our proprietary CAR technology and myeloid cell engineering technology.

Exclusively Licensed Intellectual Property — Penn

We have exclusive rights to four patent families, and non-exclusive rights to related know-how by virtue of a license agreement with the Trustees of the University of Pennsylvania, or Penn. These patent families are directed to, among other things, methods of efficiently expressing CARs in myeloid cells, including monocytes, macrophages, and dendritic cells and enhancing effector activity, as well as the modified cells and compositions including such modified cells for use in several indications including various oncology targets. The applications will have an expiration date of no earlier than 2034. This licensed patent portfolio includes:

- A patent family that includes nine issued U.S. patents and three pending U.S. patent applications relating to modified macrophages, monocytes and dendritic cells comprising CARs. These U.S. patents are expected to expire in 2036, absent any term adjustments or extensions. Corresponding foreign applications have been filed and are pending in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, Korea, Mexico, New Zealand, Russia, Singapore, Thailand and South Africa.
- A patent family that includes one pending U.S. patent application relating to modified macrophages, monocytes and dendric cells in protein aggregate-associated disorders. Patent applications in this family are expected to expire in 2039, absent any term adjustments or extensions. Corresponding foreign applications have been filed and are pending in Australia, Canada, China, Europe, Israel, Japan, Korea, New Zealand, and Singapore.
- A patent family that includes one pending U.S. patent application relating to activation of antigen presenting cells. Patent applications in this family are expected to expire in 2040, absent any term adjustments or extensions. A corresponding foreign application has been filed in Europe.
- A patent family that includes one issued U.S. patent and one pending U.S. patent application relating to CARs comprising human anti-mesothelin binding domains. Patent applications in this family are expected to expire in 2034, absent any adjustments or extensions. Corresponding foreign applications have been filed and are pending in Australia, Canada, China, Europe and Japan.

Exclusively Licensed Intellectual Property — NYU

We have exclusive rights to one patent family, and non-exclusive rights to related know-how by virtue of a license agreement with New York University, or NYU. The rights granted under the NYU license are to all indications for human use. This licensed patent portfolio includes:

- A patent family that includes one U.S. patent relating to a chimeric human immunodeficiency virus type 1, or HIV-1, vector with a simian immunodeficiency virus, or SIV, minimal Vpx packaging domain and method of making virions with enhanced infectivity for macrophages and dendritic cells. The U.S. patent is expected to expire in 2033, absent any term adjustments or extensions.

Carisma Owned Intellectual Property

We currently own seven U.S. patent families. This owned patent portfolio includes:

- A patent family that includes one issued U.S. patent and two pending U.S. patent applications relating to macrophages, monocytes and dendritic cells comprising novel CAR constructs. Patent applications in this family are expected to expire in 2041, absent any term adjustments or extensions.

- A patent family that includes one pending Patent Cooperation Treaty, or PCT, application relating to mRNA transfection of macrophages, monocytes and dendritic cells comprising CARs. Patent applications in this family are expected to expire in 2041, absent any term adjustments or extensions.
- A patent family that includes one pending PCT application relating to modified immune cells for fibrosis and inflammation. Patent applications in this family are expected to expire in 2041, absent any term adjustments or extensions.
- A patent family that includes one pending PCT application relating to self-polarizing immune cells. Patent applications in this family are expected to expire in 2042, absent any term adjustments or extensions.
- A patent family that includes one pending PCT application relating to in vivo delivery of, among other things, CARs to macrophages, monocytes, and dendritic cells.
- A patent family that includes one pending PCT application relating to methods and constructs for modifying the response of certain cells to environmental and other stimuli.
- A patent family that includes one pending PCT application relating to modified constructs including myeloid differentiation primary response protein 88, or MyD88, and/or CD40, domains.

We will also seek to generate additional intellectual property that covers enhancements to all aspects of the platform, including novel CARs, combinations, gene editing and manufacturing improvements. Where appropriate, we will also look to in-license relevant technology from third parties.

Patent Term and Patent Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or USPTO, in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre- market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims regarding the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

Trademarks

Our trademark portfolio currently includes registered U.S. trademarks for Carisma in the United States, Europe, Great Britain and Japan. All of our trademarks are renewed on an ongoing basis. In order to supplement the protection of our brand, we also have a registered internet domain name. Going forward, we will consider additional trademarks to enhance our brand and support our products.

Trade Secrets

We rely, in some circumstances, on trade secrets to protect our unpatented technology. However, trade secrets can be difficult to protect in certain circumstances. We seek to protect our trade secrets and proprietary technology and processes, including through confidentiality agreements with our employees, consultants, scientific advisors and contractors. 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. We may not have adequate remedies for any breach and could lose our trade secrets through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

Moderna Collaboration and License Agreement

In collaboration with Moderna, we have established an approach that uses Moderna's mRNA/LNP technology, together with our CAR-M platform technology, to create novel *in vivo* oncology gene therapies. We believe this approach has the potential to enable a series of off-the-shelf product candidates to target a patient's own myeloid cells against cancer cells directly within their body.

In January 2022, Legacy Carisma and Moderna established this collaboration by entering into a Collaboration and License Agreement, or the Moderna License Agreement, which provides for a broad strategic collaboration to discover, develop and commercialize *in vivo* engineered CAR-M therapeutics for up to 12 oncology programs. Under the Moderna License Agreement, the parties initiate research programs during a research term, focused on the discovery and research of products directed to biological targets. Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Moderna has the right to designate up to 12 research targets as development targets. The first five research targets have been designated and all programs are currently in the discovery phase. Moderna funds the cost of our activities in accordance with an agreed research budget.

Moderna has the right to designate up to 12 research targets as development targets during a specified development target nomination period upon payment of a development target designation milestone payment. Moderna can replace development targets with research targets during a specified period of time. If Moderna exercises its right to designate a development target, Moderna will have a worldwide, exclusive license under patents and know-how controlled by us to develop and commercialize products directed to the applicable development target, subject to certain diligence obligations.

Commencing a specified time after the effective date of the Moderna License Agreement, Moderna will have the right to nominate targets relating to diseases outside the field of oncology for inclusion in research programs in specified circumstances. Such right is subject to the same exclusions as Moderna's right to nominate other targets for inclusion in research programs.

During the term of the Moderna License Agreement, we and our affiliates are subject to various exclusivity obligations under which we are not permitted to research, develop or commercialize particular products outside of the collaboration, including products for use as *in vivo* therapies in the field of oncology, products directed to any target included in the collaboration, or products containing a polypeptide provided by us to Moderna in connection with a research program that are directed to any development target.

Under the terms of the Moderna License Agreement, we received a $45.0 million up-front cash payment. Assuming Moderna develops and commercializes 12 products, each directed to a different development target, we are also eligible to receive up to between $247.0 million and $253.0 million per product in development target designation, development, regulatory and commercial milestone payments. In addition, we are eligible to receive tiered mid-to-high single digit royalties on net product sales, subject to adjustment. Moderna has also agreed to cover the cost of certain milestone payments and royalties we owe as a licensor under one of our intellectual property in-license agreements with Penn that we are sublicensing to Moderna under the Moderna License Agreement, which royalties Moderna may deduct in part from any royalties owed to us.

Unless earlier terminated, the Moderna License Agreement will expire upon the expiration of all royalty obligations thereunder. The royalty period for each product developed under the Moderna License Agreement will expire on a country-by-country basis upon the later of (i) the expiration of the last-to-expire valid patent claim of specified patents, (ii) the expiration of regulatory-based exclusivity for such product in such country or (iii) ten years after the first commercial sale with respect to such product in such country. Moderna has the right to terminate the Moderna License Agreement for convenience in its entirety or with respect to a specific product or target on ninety days' prior notice. Either we or Moderna may terminate the Moderna License Agreement in its entirety if the other party is in material breach and such breach is not cured within the specified cure period, except in the case of Moderna's breach of its diligence obligations, termination by us is limited to the applicable target and product. In addition, either we or Moderna may terminate the Moderna License Agreement in the event of specified insolvency events involving the other party. As an alternative to termination in the event of our uncured material breach of certain sections of the agreement, Moderna has the option to continue the collaboration under the agreement with reduced payment obligations.

Penn License Agreement

In November 2017, Legacy Carisma entered into a license agreement, or the Penn License Agreement, with Penn, which was amended in February 2018, January 2019, March 2020 and June 2021. Pursuant to the Penn License Agreement, Penn granted us (i) an exclusive, worldwide license, with specified rights to sublicense, under Penn's interest in specified patents related to CAR macrophages, monocytes or dendritic cells, (ii) an exclusive, worldwide license, with specified rights to sublicense, under Penn's interest in specified patents related to CAR-M directed to mesothelin, and (iii) a nonexclusive, worldwide license under Penn's interest in specified know-how related to CAR-M, with limited rights to sublicense only in combination with specified products or patents. These licensed patents and know-how arose primarily from research conducted by Dr. Saar Gill and Dr. Michael Klichinsky at the University of Pennsylvania, co-founders of Carisma. The foregoing licenses are subject to rights retained by Penn for specified non-commercial uses and rights retained by the U.S. government. Under the Penn License Agreement, we are obligated to use commercially reasonable efforts to pursue development and commercialization of at least one CAR-M product in oncology and non-oncology fields.

We are responsible for paying Penn an annual license maintenance fee in the low tens of thousands of dollars, payable until our first payment of a royalty. We are required to pay Penn up to $10.9 million per product in development and regulatory milestone payments, up to $30.0 million per product in commercial milestone payments, and up to an additional $1.7 million in development and regulatory milestone payments for the first CAR-M product directed to mesothelin. While the agreement remains in effect, we are required to pay Penn low to mid-single digit percentage tiered royalties on annual net sales of licensed products, which may be subject to reductions. Penn is guaranteed a minimum royalty payment amount in the low hundreds of thousands of dollars for each year after the first commercial sale of a licensed product. We must also pay Penn a percentage in the mid-single digits to low double digits of certain types of income we receive from sublicensees. In addition, we are required to pay Penn an annual alliance management fee in the low tens of thousands of dollars, ending after several years, unless we provide funding to Penn for research and development activities that extend beyond a specified date, in which case we will continue to owe the alliance management fee for each year in which we continue to fund such activities. We also paid Penn an upfront fee in the low hundreds of thousands of dollars for the license to the patents related to the mesothelin binder that is incorporated into the CAR design for our mesothelin product candidate. We are responsible for a pro rata share of costs relating to the prosecution and maintenance of the licensed patents.

The royalty period for each licensed product will expire on a product-by-product basis upon the later of (i) the expiration of the last-to-expire valid patent claim of the licensed patents covering such product in the country of sale or in the country of manufacture, or (ii) the expiration of regulatory-based exclusivity for such product in the country of sale. The license agreement remains in effect until the later of (i) expiration or abandonment of the last licensed patent or (ii) loss of regulatory exclusivity. We may terminate the agreement for convenience upon thirty days' prior notice. Penn may terminate the agreement for our material breach, subject to a specified cure period, except for certain breaches for which Penn may terminate immediately. Penn may also terminate if we become the subject of a specified insolvency event.

NYU License Agreement

In July 2020, Legacy Carisma entered into a license agreement with NYU, or the NYU License Agreement. Pursuant to the NYU License Agreement, NYU granted us (i) an exclusive, worldwide license, with specified rights to sublicense, under NYU's interest in specified patents related to the Vpx-LV and (ii) a nonexclusive, worldwide license, with specified rights to sublicense, under NYU's interest in specified know-how related to the Vpx-LV, in each case to develop, manufacture, use and sell products developed using the Vpx-LV, or Licensed Products. The foregoing licenses are subject to rights retained by NYU to use, and to permit other non-commercial entities to use, the licensed patents and licensed know-how for educational and research purposes, as well as rights retained by the U.S. government. Under the NYU License Agreement, we are obligated to use reasonable diligence to carry out a specified development plan and to obtain regulatory approval for Licensed Products in the United States and each of the other countries in which we or our sublicensees intend to produce, use, and/or sell Licensed Products, as well as to begin the regular commercial production, use, and sale of the Licensed Products in good faith in accordance with the development plan and to continue diligently thereafter to commercialize the Licensed Products.

We are required to pay NYU an annual license maintenance fee in the mid tens of thousands of dollars; up to $1,685,000 per Licensed Product in development and regulatory milestone payments; and low single digit percentage tiered royalties on annual net sales of Licensed Products on a country-by-country basis until the later of (i) 12 years after first commercial sale of a Licensed Product in such country or (ii) expiration of the last to expire licensed patent. We must also pay NYU a percentage in the low single digits to low double digits of certain types of income we receive from sublicensees or

assignees of the agreement. We are also responsible for all costs relating to the prosecution, maintenance, and defense of the licensed patents.

The NYU License Agreement remains in effect until the expiration of all royalty terms in all countries. Either party may terminate the NYU License Agreement for the other party's uncured material breach or insolvency or bankruptcy.

Competition

The biopharmaceutical industry, and in particular the cell therapy field, is characterized by intense investment and competition aimed at rapidly advancing new technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. Our platform and therapeutic product candidates are expected to face substantial competition from multiple technologies, marketed products, and numerous other therapies being developed by other biopharmaceutical companies, academic research institutions, governmental agencies, and public and private research institutions. Many of our potential competitors have substantially greater financial, technical, and other resources, such as larger research and development staff, established manufacturing capabilities and facilities, and experienced marketing organizations with well-established sales forces, and any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. In addition, there is substantial patent infringement litigation in the biopharmaceutical industry, and, in the future, we may bring or defend such litigation against our competitors.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience and price, the level of competition, and the availability of coverage and adequate reimbursement from third-party payors.

Unlike other cell therapy approaches, our CAR-M platform is based on engineering macrophages and monocytes with proprietary vectors, constructs, and processes, enabling a differentiated platform from other cell therapy competitors that primarily focus on T or natural killer cells, or NK cells. While we believe that our scientific expertise, novel technology, and intellectual property position offer competitive advantages, we face competition from multiple other cell therapy technologies and companies. Other companies developing engineered myeloid cell therapies include, among others, Myeloid Therapeutics, Shoreline Biosciences, Inceptor Bio, Thunder Bio, Resolution Therapeutics, CellOrigin, Deverra, SIRPant Therapeutics, and others.

Due to the broad promise of cell therapies, and the potential of myeloid cell-based approaches to expand cell therapy efficacy into solid tumors, we expect increasing competition from new and existing companies across several fronts, which include, among others:

- ***Myeloid cell therapies:*** CellOrigin, Deverra, Inceptor Bio, Myeloid Therapeutics, Resolution Therapeutics, Shoreline Biosciences, Thunder Bio, among others
- ***Autologous* T cell *therapies:*** 2seventy, Adaptimmune, Autolus, Bristol Myers Squibb, Cabaletta, Gracell, Kite/ Gilead, Novartis, Poseida, TScan, Vor, among others
- ***Allogeneic* T cell *therapies:*** Allogene, Atara, Caribou, Century, Cellectis, Celyad, CRISPR, Fate, Gracell, Kite/ Gilead, Legend, Poseida, Precision Bio, Sana, TScan, Vor, among others
- ***NK and other cell therapies:*** Adicet, Artiva, Celularity, Century, Editas, Fate, Fortress, Gamida Cell, ImmunityBio, Nkarta, NKGen, Takeda, among others
- ***Direct in vivo reprogrammed cell therapies:*** BioNTech, Ensoma, Interius, Sanofi, Umoja, Orna Therapeutics, among others

In addition to competition from other cell therapy companies, any products that we develop may also face competition from other types of therapies. Other companies developing non-cell therapies, including gene therapies, in relevant therapeutic areas include Gilead, ALX Oncology, Five-Prime, Immune-Onc, Pionyr, Infinity, NextCure, OncoResponse, Curis, Faron, Apexigen, Pfizer, Dren, and multiple biotechnology and pharmaceutical companies developing other directly competitive technologies such as small molecules, immune agonists, antibodies, bi/tri specific antibodies, antibody drug conjugates, and other solid tumor therapeutics.

We also compete with third parties for retaining qualified scientific 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. We may pursue the in-license or acquisition of rights to complementary technologies and product candidates on an opportunistic basis. The acquisition and licensing of technologies and product candidates is a competitive area, and a

number of more established companies also have similar strategies to in-license or acquire technologies and product candidates that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the relevant technology or product candidate on terms that would allow it to make an appropriate return on our investment.

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. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before it is able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our product candidates are regulated as biological products, or biologics, under the Public Health Service Act, or the PHSA, and the Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations and guidance. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable U.S. requirements at any time during the product development process, including pre-clinical testing, clinical testing, the approval process, or post-approval process, may subject a sponsor to delays in the conduct of the study, regulatory review, and approval, and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- pre-clinical laboratory tests, animal studies, and formulation studies all performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards and other applicable regulations;
- completion of the manufacture, under current good manufacturing practice, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current IND or good clinical practice, or GCP;
- preparation and submission to the FDA of a Biologic License Application, or BLA, for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the chemistry, manufacturing and controls, or CMC, for the product in clinical development and proposed labelling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity;
- satisfactory completion of any FDA audits of the pre-clinical studies and clinical trial sites to assure compliance with GLP, as applicable, and GCP, and the integrity of clinical data in support of the BLA;

- payment of user Prescription Drug User Fee Act, or PDUFA fees, securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and any post-approval studies or other post-marketing commitments required by the FDA.

Pre-clinical Studies

Before testing any biologic product candidate in humans, the product candidate must undergo pre-clinical testing. Pre-clinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. These studies are often referred to as IND-enabling studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

Investigational New Drug Application

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks or any issues surrounding CMC for the proposed product. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin or recommence. As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND.

If the FDA raises concerns or questions either during this initial 30-day period, or at any time following allowance of an IND, it may choose to impose a partial or complete clinical hold. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, pre- clinical, and/or CMC. This order issued by the FDA would delay either a proposed clinical trial or cause suspension of an ongoing trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing a planned clinical trial or future clinical trials in a timely manner.

Following the issuance of a clinical hold or partial clinical hold, a clinical investigation may only resume once the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed or recommence.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation,

conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, if a sponsor has a policy regarding how it evaluates and responds to expanded access requests, sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition to and separate from expanded access, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease or condition to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, or DSMB. This group may recommend continuation of the trial as planned, changes in trial conduct, or cessation of the trial at designated check points based on certain available data from the trial to which only the DSMB has access.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.
- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve a BLA for a product but require the sponsor to conduct additional clinical trials to further assess the product's safety and effectiveness after approval. Such trials are typically referred to as post approval or

post marketing clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any post marketing clinical trial requirement or to request a change in the product labeling. The failure to exercise due diligence with regard to conducting post approval clinical trials could result in withdrawal of approval for products.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. In January 2024, the FDA issued draft guidance setting out its policies for the collection of race and ethnicity data in clinical trials.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry, clinicaltrials.gov, maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The FDA has issued several pre-notices for voluntary corrective action and several notices of non-compliance during the past two years. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Clinical Studies Outside the United States in Support of FDA Approval

In connection with a clinical development program, a sponsor may conduct trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of U.S. approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers

such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect and more frequently if serious adverse events occur. These reports must include a development safety update report, or DSUR. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other trials or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, there are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-BLA meetings, as well as end of phase meetings such as End of Phase 2, or EOP2, meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product. A Type D meeting is focused on a narrow set of issues, which should be limited to no more than two focused topics, and should not require input from more than three disciplines or divisions. Finally, INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs, or INTERACT, meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Special Regulations and Guidance Governing Gene Therapy Products

The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which is administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the FDA has established the Office of Tissues and Advanced Therapies, or the OTAT, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. In September 2022, the FDA announced renaming of the OTAT to the Office of Therapeutic Products, or the OTP, and elevation of the OTP to a "Super Office" to meet its growing cell and gene therapy workload and new commitments under the PDUFA for fiscal years 2023 to 2027.

The FDA has issued various guidance documents regarding gene therapies, including final guidance documents released in January 2020 relating to CMC information for gene therapy INDs, gene therapies for rare diseases and gene therapies for retinal disorders, as well as draft guidance in January 2021 for Human Gene Therapy for Neurodegenerative Diseases. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, we believes that our compliance with them is likely necessary to gain approval for any gene therapy product candidate we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper pre-clinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure

product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

Finally, for a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with good tissue practices, or GTP. These standards are found in FDA regulations and guidance that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that T cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product 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. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are completed. The FDA is required to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA. Further, Section 505B of the FDCA, as amended by the FDA Reauthorization Act of 2017, or FDARA, requires that any original NDA or BLA submitted on or after August 18, 2020, for a new active ingredient, must contain reports on the molecularly targeted pediatric cancer investigation, unless the requirement is waived or deferred, if the drug that is the subject of the application is: (i) intended for the treatment of an adult cancer, and (ii) directed at a molecular target that the Secretary determines to be substantially relevant to the growth or progression of a pediatric cancer in accordance with FDA guidance. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Compliance with cGMP Requirements

Concurrent with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, and purity of the finished product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. The Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act, or PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Submission and Review of a BLA

The results of product candidate development, pre-clinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2024 is $4,048,695 for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for federal fiscal year 2024 is $416,734. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of a BLA, the FDA has 60 days to conduct a preliminary review of the application and it must inform the sponsor within that period of time whether the BLA is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information and studies, and the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the sponsor, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

In connection with its review of a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. With passage of the FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspections of facilities involved in the preparation,

conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides 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.

The FDA also may require submission of a risk evaluation and mitigation strategies, or REMS, if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, or ETASU, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

The FDA's Decision on a BLA

Under the Provincial Health Services Authority, or PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent, and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent. Specifically, the FDA must determine that the expected benefits of the proposed product outweigh its potential risks to patients. This "benefit- risk" assessment is informed by the extensive body of evidence about the proposed product in the BLA. On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of pre-clinical and clinical trial sites to assure compliance with GCPs, the FDA may issue a complete response letter, or CRL, or an approval letter.

If the application is not approved, the FDA will issue a CRL, which will contain the conditions that must be met in order to secure final approval of the application and will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a CRL may submit to the FDA information that represents a complete response to the issues identified by the FDA, withdraw the application or request a hearing. The FDA will not approve an application until issues identified in the CRL have been addressed. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six-month extension to respond.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. The FDA may limit the approved indication(s) for use of the product. It may also require that contraindications, warnings, or precautions be included in the product labeling. In addition, the FDA may call for post -approval studies, including Phase 4 clinical trials, to further assess the product's efficacy and/or safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

- *Fast Track designation*. The sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if *they* are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.
- *Breakthrough therapy designation*. To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.
- *Priority review*. A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.
- *Accelerated approval*. Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.
- In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.
- *Regenerative advanced therapy*. With passage of the Cures Act, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of 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 ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a biologic product. Products may be promoted only for the approved indications 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, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the U.S. Department of Health and Human Services, or the HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

Although physicians may prescribe legally available products for unapproved uses or patient populations, or "off-label uses, manufacturers may not market or promote such uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in non-promotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Under Omnibus legislation enacted in December 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA. In addition, the FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent exclusivity in the United States and for biologics, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing regulatory exclusivity, including orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity that cover the product are extended by six months.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, or ACA, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. A biosimilar is a biological product that is highly similar to an existing FDA-licensed "reference product." The FDA has approved a number of biosimilar products and interchangeable biosimilar products.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and

proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

An application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

Federal and State Data Privacy and Security Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the Health Insurance Portability and Accountability Act, or HIPAA, the HHS, has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans, and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In 2018 California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020, and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency—the California Privacy Protection Agency—whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, eleven other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the

2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024.

Patent Term Restoration and Extension

In the United States, a patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND clearing clinical studies and the submission date of the BLA, plus the time between the submission date of the BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

FDA Approval of Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products. The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple biological oncology products, when appropriate. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, pre-clinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and pre-clinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the sponsor must prepare

and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2024, the standard fee is $483,560 and the small business fee is $120,890.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates a sponsor may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates a sponsor may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates a sponsor may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on a sponsor's sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable a sponsor to maintain price levels sufficient to realize an appropriate return on a sponsor's investment in product development. In addition, any companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to any companion diagnostics.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on 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 a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates a sponsor may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a sponsor to conduct a clinical trial that compares the cost effectiveness of any product candidates a sponsor may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in a sponsor's commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health

insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or they may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of a sponsor's products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain a sponsor's business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government;
- the Foreign Corrupt Practices Act, or the FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and
- the federal transparency requirements under the ACA, which require certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or the CMS, within the HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. In addition, certain state and local laws require drug manufacturers to register pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If a sponsor's operations are found to be in violation of any of these laws or any other governmental regulations that may apply to a sponsor, a sponsor may be subject to significant civil, criminal, and administrative penalties, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of a sponsor's operations.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the U.S. Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief and Economic Security Act, or the CARES Act.

The American Taxpayer Relief Act of 2012, which was enacted in January 2013, among other things, further reduced Medicare payments to several 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. Further, with passage of the Inflation Reduction Act in August 2022, or IRA, Congress extended the expansion of ACA premium tax credits through 2025. Those subsidies were originally extended through 2022 under the American Rescue Plan Act of 2021. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices a sponsor may obtain for any of a sponsor's product candidates for which a sponsor may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019 Further, on June 17, 2021, the U.S. Supreme Court dismissed a lawsuit after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump administration took executive actions to undermine or delay implementation of the ACA, but those actions were rescinded with issuance of an Executive Order on January 28, 2021, by President Biden which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the CMS issued a final rule to rescind it. With issuance of this rule, the CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation.

Further, on November 20, 2020, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The IRA, further delayed implementation of this rule to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

On August 16, 2022, the IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. 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 HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. The CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 additional Part D drugs in 2027, 15 additional Part B or Part D drugs in 2028, and 20 additional Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

Further, with passage of the IRA in August 2022, Congress authorized Medicare beginning in 2026 to negotiate lower prices for certain costly single- source drug and biologic products that do not have competing generics or biosimilars. This provision is limited in terms of the number of pharmaceuticals whose prices can be negotiated in any given year and it only applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years. Drugs and biologics that have been approved for a single rare disease or condition are categorically excluded from Medicare price negotiations. Further, the new legislation provides that if pharmaceutical companies raise prices in Medicare faster than the rate of inflation, they must pay rebates back to the government for the difference. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and the CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce (the "Chamber"), Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and the CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing 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. A number of states, for example, require pharmaceutical manufacturers and other entities in the supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. 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. These measures could reduce the ultimate demand for a sponsor's products, once approved, or put pressure on a sponsor's product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Human Capital

Employee Matters

As of December 31, 2023, we had 107 full-time employees, including a total of 33 employees with M.D. or Ph.D. degrees, all of whom are located in the United States. Of these full-time employees, 93 are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital objectives are focused on attracting, developing, and retaining talent. Cash compensation plans, comprehensive benefits plans and equity grants are designed to attract, retain and to motivate employees, directors, and select consultants to achieve our corporate objectives. We also provide for employer matching contributions equal to 100% of employee deferral contributions up to a deferral rate of 5% of eligible compensation to our Section 401(k) retirement savings plan.

Cost Reduction Measures

We have recently taken steps to reduce our operating expenses and conserve cash as we focus our development efforts on high potential value programs with meaningful near-term milestones. As described in Part II, Item 9B of this Annual Report on Form 10-K, in late March 2024, our board of directors approved a reduction in force of 39 full-time employees (representing approximately 37% of our total workforce), including certain employees engaged in research and development activities and certain finance and corporate employees. We believe these changes will provide operating efficiencies for us to continue to support our product development programs as well as any potential collaborations or other strategic relationships we may enter into.

Our Corporate Information

Our principal executive offices are located at 3675 Market Street, Suite 200, Philadelphia, PA, and our telephone number is (267) 491-6422. Our website address is *httpp://www.carismatx.com*. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

We own or have rights to, or have applied for, trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for

convenience, some of the trademarks, service marks and trade names referred to in this Annual Report on Form 10-K are listed without the ® and ™ symbols.

Available Information

We make available, through our website *httpp://www.carismatx.com*, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended as soon as reasonably practicable after we electronically file such material with the Securities and Exchange Commission, or the SEC. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors set forth below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes and the section of this Annual Report on Form 10-K titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase our securities. The risks and uncertainties we describe below and in the documents mentioned above are not the only ones we face. Additional risks and uncertainties not presently known to us could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment.

Summary of Risk Factors

- We have incurred significant losses since our inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding for our continuing operations. Attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our discovery and product development efforts.
- We have never generated revenue from product sales and may never achieve or maintain profitability.
- Our reduction in force undertaken to extend our cash runway and focus our resources on our prioritized research and development programs might not achieve our intended outcome.
- We are heavily dependent on the success of our follow-on product candidate, CT-0525, which will require significant clinical testing before we can seek marketing approval and potentially generate commercial sales. If CT-0525 does not receive marketing approval or is not successfully commercialized, or if there is significant delay in doing so, our business will be harmed.
- We will need substantial additional funding for our continuing operations. If we are unable to raise additional capital when needed or on acceptable terms, we could be forced to further delay, reduce or eliminate our discovery or product development programs or commercialization efforts.
- Cell therapy is a rapidly evolving area of science, and the approach we are taking to discover and develop product candidates by utilizing genetically modified macrophages is novel and may never lead to approved or marketable products.
- We have and may in the future curtail, pause, delay or cease development of a product candidate at any stage of pre-clinical or clinical development based on a variety of factors, including our judgments regarding costs or timing of further development, probability of success of clinical development, regulatory requirements, commercial potential, relative benefits and costs compared to other product candidates in our portfolio, and our overall corporate strategy.
- Even if any of our product candidates receives marketing approval, we 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, and the market opportunity for any of our product candidates, if approved, may be smaller than we estimate.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may prevent or delay our ability to seek or obtain marketing approval for or commercialize our product candidates or otherwise harm our business. If we are not able to maintain these third-party relationships or if these arrangements are terminated, we may have to alter our development and commercialization plans and our business could be adversely affected.

- We rely, and expect to continue to rely, on third parties to conduct our manufacturing of our drug substance and drug product, and those third parties may not perform satisfactorily, including failing to meet deadlines to provide adequate drug product for our clinical trials. This may prevent or delay our ability to complete our clinical trials and to seek or obtain marketing approval for or commercialize our product candidates or otherwise harm our business. If we are not able to maintain these third-party relationships or if these arrangements are terminated, we may have to alter our development and commercialization plans and our business could be adversely affected.
- If we are unable to obtain, maintain and enforce patent protection for our technology and product candidates or if the scope of the patent 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 and we may not be able to compete effectively in our market.
- The regulatory approval process of the FDA is lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.
- The market price of our common stock may be volatile, and the market price of our common stock may drop in the future.
- We incur and will continue to incur additional costs and increased demands upon management as a result of complying with the laws and regulations affecting public companies.
- If at some point we are no longer a "smaller reporting company" or otherwise no longer qualify for applicable exemptions, we will be subject to additional laws and regulations affecting public companies that will increase our costs and the demands on management and could harm our operating results.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future, and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $86.9 million and $61.2 million for the years ended December 31, 2023 and 2022, respectively. To date, we have not yet commercialized any products or generated any revenue from product sales and have financed our operations primarily with proceeds from sales of our preferred stock, proceeds from our collaboration with Moderna, research tax credits and convertible debt financing. We have devoted substantially all of our financial resources and efforts to pursuing discovery, research and early clinical development of our product candidates. We are in the early stages of development of our follow-on product candidate, CT-0525, and expect to treat the first patient in the second quarter of 2024.

We expect to continue to incur significant expenses and operating losses for the foreseeable future, including costs associated with operating as a public company. We anticipate that our expenses will increase substantially if and as we:

- enhance the capabilities of our CAR-M platform;
- conduct a planned clinical trial of CT-0525 for solid tumors that over-express HER2;
- conduct our ongoing Phase 1 clinical trial of CT-0508 with respect to patients currently enrolled or in screening;
- conduct our sub-study of our ongoing Phase 1 clinical trial utilizing CT-0508 in combination with pembrolizumab with respect to patients currently enrolled or in screening;
- conduct discovery and pre-clinical testing of the development of *in vivo* CAR-M therapeutics for up to twelve oncology targets, as well as multiple other targets and indications;
- conduct discovery and pre-clinical testing of our autologous cell therapy pipeline to gather information to apply to the development of off-the-shelf engineered macrophage therapeutics;
- develop iPSC-derived CAR-M, and other macrophage therapies;
- develop *in vivo* reprogrammed mRNA/LNP CAR-M therapies for cancer;
- develop viral vectors to effectively engineer human monocytes and macrophages, including the Vpx lentiviral vector and our Ad5f35 vector;
- conduct discovery and pre-clinical testing of our other product candidates;
- seek marketing approval for CT-0525 or any other product candidate if we successfully complete clinical trials;
- scale up our external manufacturing capabilities and capabilities to support clinical trials of CT-0525 or any other of our product candidates and for commercialization of any product candidate for which we may obtain marketing approval;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- in-license or acquire additional technologies or product candidates;

- make any payments under our existing or future strategic collaboration agreements, global exclusive rights licensing agreements or sponsored research agreements, including with Moderna, Penn and NYU;
- maintain, expand, enforce and protect our intellectual property portfolio;
- hire additional clinical, regulatory, manufacturing, quality control, development and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our discovery, product development and planned future commercialization efforts and our operations as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Our expenses could increase beyond our expectations if, among other things:

- we are required by regulatory authorities in the United States, Europe or other jurisdictions to perform trials or studies in addition to, or different than, those that we currently expect;
- there are any delays in establishing appropriate manufacturing arrangements for or completing the development of any of our product candidates; or
- there are any third-party challenges to our intellectual property or our needs to defend against any intellectual property-related claim.

Even if we obtain marketing approval for and are successful in commercializing one or more of our product candidates, we expect to incur substantial additional discovery and product development and other expenditures to develop and market additional product candidates or to expand the approved indications of any marketed product. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

We have never generated revenue from product sales and may never achieve or maintain profitability.

We recently initiated clinical development of our follow-on product candidate, CT-0525. Other than completing remaining activities under our ongoing Phase 1 clinical trial of CT-0508 with respect to patients currently enrolled or in screening, we are in the pre-clinical testing stages for our other product candidates. We expect that it will be a number of years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must succeed in completing development of, obtaining marketing approval for and eventually commercializing, one or more products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing clinical development of CT-0525, completing discovery, pre-clinical testing and clinical development of CT-0525 in the combination setting and for additional indications, timely filing and receiving acceptance of our IND applications, in order to commence our planned or future clinical trials, successfully enrolling subjects in, and completing, our ongoing and planned clinical trials, scaling up our manufacturing processes and capabilities to support clinical trials of CT-0525 or of other product candidates, obtaining marketing approval for CT-0525 or any other product candidates, manufacturing, marketing and selling any products for which we may obtain marketing approval and maintaining a continued acceptable safety profile of our products following approval. We may never succeed in these activities and, even if we do, we may never generate revenues that are significant enough to achieve profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our discovery and product development efforts, diversify our pipeline of product candidates or even continue our operations.

We are heavily dependent on the success of our follow-on product candidate, CT-0525, which will require significant clinical testing before we can seek marketing approval and potentially generate commercial sales. If CT-0525 does not receive marketing approval or is not successfully commercialized, or if there is significant delay in doing so, our business will be harmed.

We initiated our first clinical trial in 2021, have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures for the foreseeable future will be devoted to CT-0525 and related combination sub-studies, including CT-0525 in combination with pembrolizumab. Our business currently depends heavily on the successful development, marketing approval and commercialization of CT-0525, and the success of related combination sub-studies. We cannot be certain that CT-0525 or

any combination therapy involving CT-0525 will achieve success in ongoing or future clinical trials, receive marketing approval or be successfully commercialized.

If we were required to discontinue development of CT-0525, or if CT-0525 does not receive marketing approval for one or more of the indications we pursue, fail to achieve significant market acceptance, or fail to receive adequate reimbursement, we may be delayed by many years in our ability to achieve profitability, if ever, and may not be able to generate sufficient revenue to continue our business.

We will need substantial additional funding for our continuing operations. If we are unable to raise additional capital on acceptable terms, we could be forced to further delay, reduce or eliminate our discovery or product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct our ongoing clinical trial of CT-0525 and pursue related combination strategies, prepare for, initiate and conduct clinical trials of other product candidates, advance our discovery programs and continue our product development efforts. We expect our expenses to increase substantially over time in connection with our ongoing activities, particularly as we advance our pre-clinical activities and clinical trials. In addition, if we obtain marketing approval for CT-0525 or any other product candidate we are developing or develop in the future, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, we will incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise additional capital or obtain adequate funds on acceptable terms, we may be required to further delay, limit, reduce or terminate our discovery and product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our discovery and product development efforts.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our clinical trials of CT-0525 and other planned and future clinical trials;
- the costs of our clinical trials of CT-0508 with respect to patients currently enrolled or in screening;
- the scope, progress, costs and results of pre-clinical testing and clinical trials of CT-0525 for additional combinations, targets and indications;
- the number of and development requirements for additional indications for CT-0525 or for any other product candidates;
- the success of our collaborations with Moderna or others;
- our ability to scale up our manufacturing processes and capabilities to support clinical trials of CT-0525 and other product candidates we are developing and develop in the future;
- the costs, timing and outcome of regulatory review of CT-0525 and other product candidates we are developing and may develop in the future;
- potential changes in the regulatory environment and enforcement rules;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment of license fees and other costs of our technology license arrangements;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for CT-0525 and other product candidates we are developing and may develop in the future for which we may receive marketing approval;
- our ability to obtain and maintain acceptance of any approved products by patients, the medical community and third-party payors;
- the amount and timing of revenue, if any, received from commercial sales of CT-0525 and any other product candidates we are developing or develop in the future for which we receive marketing approval;
- potential changes in pharmaceutical pricing and reimbursement infrastructure;
- the availability of raw materials for use in production of our product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we in-license or acquire additional technologies or product candidates.

As of December 31, 2023, we had cash and cash equivalents of $77.6 million that we believe are sufficient to sustain our planned operations and capital expenditure requirements into the third quarter of 2025. However, we have based this

estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. In addition, changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. As a result, we could deplete our capital resources sooner than we currently expect. In addition, because the successful development of CT-0525 and any combination studies or other product candidates that we pursue is highly uncertain, at this time we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of any product candidate.

Identifying potential product candidates and conducting pre-clinical and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. We will not generate commercial revenues unless and until we can achieve sales of products, which we do not anticipate for a number of years, if at all. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all, and we may be impacted by the economic climate and market conditions. For example, market volatility resulting from general U.S. or global economic or market conditions, including related to any health epidemics, pandemics or other contagious outbreaks (including any resurgence of the COVID-19 pandemic), could also adversely impact our ability to access capital as and when needed. Alternatively, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We were formed as Carma Therapeutics LLC, a Pennsylvania limited liability company, in April 2016 and converted to a Delaware corporation in May 2017 under the name CARISMA Therapeutics Inc. In connection with the Merger consummated in March 2023, CARISMA Therapeutics Inc. merged with and into a wholly-owned subsidiary of Sesen Bio and was renamed "CTx Operations, Inc." Sesen Bio's name was changed to "Carisma Therapeutics Inc." Following the completion of the Merger, the business conducted by the public company became primarily the business conducted by us. We are a clinical-stage cell therapy company with a limited operating history. Cell therapy product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations prior to the Merger have been limited to organizing and staffing the company, business planning, capital raising, establishing and maintaining our intellectual property portfolio, building our pipeline of product candidates, conducting drug discovery activities, undertaking pre-clinical studies, manufacturing process development studies, conducting early-stage clinical trials, and providing general and administrative support for these operations. Our prospects must be considered in light of the uncertainties, risks, expenses and difficulties frequently encountered by companies in their early stages of operations. We have not yet demonstrated our ability to successfully develop any product candidate, obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make 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 products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown obstacles. We will need to transition at some point from a company with a discovery and pre-clinical and clinical focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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 quarterly or annual periods as indications of future operating performance.

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law. Prospective investors should consult

their tax advisors regarding the potential consequences of changes in tax law on our business and on the ownership and disposition of our common stock.

Our ability to use our net operating loss carryforwards, or NOLs, and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

Prior to the Merger, we had a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future. As a result, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards. As of December 31, 2023, we had federal, state and local NOLs of $317.6 million, $229.4 million and $40.8 million, respectively, and federal research and development tax credit carryforwards totaling $9.9 million.

In general, under Section 382 of the Code and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a three-year period, is subject to limitations on our ability to utilize our pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future (which may be outside our control). As a result, if and to the extent we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

Risks Related to Our Discovery Programs and Research and Development of Our Product Candidates

Cell therapy is a rapidly evolving area of science, and the approach we are taking to discover and develop product candidates by utilizing genetically modified macrophages is novel and may never lead to approved or marketable products.

Cell therapy has yet to be broadly applied to solid tumors, inflammatory disease, fibrotic disease or neurodegeneration. The discovery, research and development of engineered macrophages to treat disease is an emerging field and our CAR-M platform, which is the first CAR-M to be evaluated in a human clinical trial, is a relatively new technology. Our future success depends on the successful development of this novel therapeutic approach. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. We have only preliminary results from our Phase 1 clinical trial of CT-0508 and expect clinical data updates in the second quarter of 2024. As such, there may be adverse effects or limited favorable results from treatment with any of our current or future product candidates that we cannot predict at this time.

Our success also depends on our successful application of our proprietary macrophage engineering platform in the combination setting and to other indications by reprogramming the target specificity of our CAR-M cell product and developing product candidates against a plethora of tumor associated antigens, including in therapeutic areas beyond oncology. However, our macrophage engineering platform may not allow us to generate new INDs to expand our pipeline on our anticipated timeline or in a cost-efficient manner or at all, which could cause the potential value of our business to decline and materially harm our business prospects.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of macrophage engineering platform will result in the development and marketing approval of any products. Any development problems we experience in the future related to our macrophage engineering platform or any of our discovery programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our clinical trials or pre-clinical studies or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

We are early in our development efforts. If we are unable to commercialize our product candidates or experiences significant delays in doing so, our business will be materially harmed.

We are early in our development efforts. We initiated our first Phase 1 clinical trial of CT-0508 in 2020. We received a Study May Proceed notification from the FDA for CT-0525 in November 2023, and expect to treat our first patient in a Phase 1 clinical trial in the second quarter of 2024.

Our ability to generate revenues from product sales, which we do not expect will occur for a number of years, if ever, will depend heavily on the successful development, marketing approval and eventual commercialization of CT-0525, including in the combination setting, or one or more of our other product candidates, which may never occur. The success of CT-0525 and our other product candidates will depend on many factors, including the following:

- successfully completing pre-clinical studies;
- successfully initiating future clinical trials;
- successfully enrolling patients in our Phase 1 clinical trial of CT-0525 and completing clinical trials;
- scaling up manufacturing processes and capabilities to support clinical trials of CT-0525 and any other product candidate;
- applying for and receiving marketing approvals from applicable regulatory authorities;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for CT-0525 and any other product candidates we are developing or may develop in the future;
- making arrangements with third-party manufacturers, or establishing commercial manufacturing capabilities, for both clinical and commercial supplies of our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of CT-0525 and any other product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- maintaining, enforcing, defending and protecting our rights in our intellectual property portfolio;
- not infringing, misappropriating or otherwise violating others' intellectual property or proprietary rights; and
- maintaining a continued acceptable safety profile of our products following receipt of any marketing approvals.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which would materially harm our business. As a company, we have limited experience in clinical development. Any predictions about the future success or viability of CT-0525 or any product candidates we are developing or may develop in the future may not be as accurate as they could be if we had a history of conducting clinical trials.

Drug development involves a lengthy and expensive process, with an uncertain outcome. The results of pre-clinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of CT-0525 or our other product candidates.

We initiated our first clinical trial of CT-0508 in 2020, and expect to dose the first patient in a Phase 1 clinical trial of CT-0525 in the second quarter of 2024. Our other product candidates are in pre-clinical development. The risk of failure for CT-0525 and our other product candidates is high. It is impossible to predict when or if CT-0525 or any of our other product candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of a product candidate, we must complete pre-clinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidate in humans. Clinical trials may fail to demonstrate that CT-0525 or any of our other product candidates are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive pre-clinical testing and studies, manufacturing process development studies, and analytical development studies that support our planned INDs and other applications to regulatory authorities in the United States or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our pre-clinical testing and studies and cannot predict if the outcome of our pre-clinical testing and studies will ultimately support the further development of our current or future product candidates or whether regulatory authorities will accept our proposed clinical programs. As a result, we may not be able to submit applications to initiate clinical development of product candidates on the timelines we expect, if at all, and the submission of these applications may not result in regulatory authorities allowing clinical trials to begin. Furthermore, product candidates are subject to continued pre-clinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. We cannot guarantee that any of our clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, among other things, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates or cause regulatory authorities to require additional testing before approving any of our product candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or at all;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may determine that the planned design of our clinical trials is flawed or inadequate;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities consider likely to predict clinical benefit;
- pre-clinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional pre-clinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain marketing approval;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our clinical investigators, regulators or IRBs to suspend or terminate the trials;
- regulators may withdraw their approval of a product or impose restrictions on its distribution; and
- business interruptions resulting from any health epidemics, pandemics or other contagious outbreaks (including any resurgence of the COVID-19 pandemic) may result in adverse effects on our business and operations.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive, if there are safety concerns or if we determine that the observed safety or efficacy profile would not be competitive in the marketplace, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;

- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in pre-clinical studies or clinical trials or in obtaining marketing or other regulatory approvals. We do not know whether any of our pre-clinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses or delays. Significant pre-clinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. 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 be impacted. For example, in December 2022, with the passage of the FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Similarly, the regulatory landscape related to clinical trials in the European Union recently evolved. The EU Clinical Trials Regulation, or the EU-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 EU-CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The EU-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 study development may proceed. If we are not able to adapt to these and other changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Further, cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for second-line or third-line use. When cancer is detected early enough, first-line therapy, usually hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. For any of our products that prove to be sufficiently beneficial, we would expect to seek approval potentially as a first-line therapy, but any product candidates we develop, even if approved, may not be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

We may conduct clinical trials at sites outside the United States. The FDA may not accept data from trials conducted in such locations, and the conduct of trials outside the United States could subject us to additional delays and expense.

We may conduct one or more clinical trials with one or more trial sites that are located outside the United States. The acceptance by the FDA or other regulatory authorities of study data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the U.S. also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

The results of early-stage clinical trials and pre-clinical studies may not be predictive of future results. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

The outcome of pre-clinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of a clinical trial do not necessarily predict final results. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. In particular, the small number of patients in our ongoing or future early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. For example, even if successful, the results of our Phase 1 clinical trial of CT-0525 may not be predictive of the results of further clinical trials of CT-0525 or any of our other product candidates. Our product candidates may also fail to show the desired safety and efficacy in clinical development despite positive results in pre-clinical studies or having successfully advanced through initial clinical trials.

Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our current or future clinical trials may not ultimately be successful or support further clinical development of any of our product candidates and we cannot assure you that any clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to support marketing approval. There is a high failure rate for product candidates proceeding through clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials even after achieving promising results in pre-clinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Any such setbacks in our clinical development could materially harm our business and results of operations.

Interim and preliminary results from our clinical trials that we announce or publish from time to time may change as more participant data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

From time to time, we may announce or publish interim or preliminary results from our clinical trials, including our Phase 1 clinical trials of CT-0508 and CT-0525. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as participant enrollment continues and more participant data become available. 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 evaluate all data. Preliminary or interim results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could be material and could significantly harm our reputation and business prospects and may cause the trading price of our common stock to fluctuate significantly.

If we experience delays or difficulties in the enrollment of patients in our clinical trials for CT-0525 or any of our other product candidates, our receipt of necessary marketing approvals could be delayed or prevented.

Identifying and qualifying patients to participate in our clinical trial for CT-0525 and any other product candidates in the future is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, our clinical trial of CT-0525 is open for enrollment and the first patient is expected to be treated in the second quarter of 2024. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols;
- the availability of existing treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials;
- the ability to identify specific patient populations based on specific genetic mutations or other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents;
- the proximity and availability of clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications or address the same patient populations as our product candidates;
- the cost to, or lack of adequate compensation for, prospective patients; and
- the impact of any health epidemics, pandemics or other contagious outbreaks (including any resurgence of the COVID-19 pandemic).

Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary marketing approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which could cause the value of our business to decline and limit our ability to obtain additional financing.

If serious adverse events, undesirable side effects or unexpected characteristics are identified during the development of CT-0525 or any of our other product candidates, we may need to abandon or limit our further clinical development of those product candidates.

The first site has been activated for the Phase 1 clinical trial of CT-0525 and the first patient is expected to be treated in the second quarter of 2024. If CT-0525 or any other product candidate is associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or pre-clinical testing, we may need to abandon development of such product candidate or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or unexpected characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound or decrease the size of the patient population for whom the compound could ultimately be prescribed. For example, while CT-0508 has been generally well tolerated based on preliminary clinical results from our Phase 1 clinical trial, such results may not be predictive or indicative of the preliminary clinical results from our Phase 1 clinical trial of our follow-on product candidate, CT-0525, or the successful development, marketing approval and eventual commercialization of CT-0525.

Additionally, if results of our clinical trials reveal undesirable side effects, we, regulatory authorities or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials, regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications or we could be forced to materially modify the design of our clinical trials. Treatment-related side effects could also affect patient

recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff.

In late March 2024, we determined to suspend enrollment of new patients in Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, in line with the clinical judgment of the clinical site principal investigator, and pause further development of CT-1119 for expense reduction purposes. If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate revenues from sales of such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

We only recently initiated clinical development of our first product candidate, CT-0508, and are initiating our first clinical trial of CT-0525 with the first patient expected to be treated in the second quarter of 2024. We are in the pre-clinical testing stages for our other product candidates. Clinical trials will be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives marketing approval, and we, or others, later discover that they are less effective than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label;
- requirement that we implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on discovery programs and product candidates that we identify for specific indications. As a result, we have and may in the future forego or delay the pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. In late March 2024, we determined to focus our *ex vivo* oncology clinical development efforts on our follow-on product candidate CT-0525, suspend enrollment of new patients in our Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, in line with the clinical judgment of the clinical site principal investigator, and pause further development of CT-1119 for expense reduction purposes. We may further curtail, pause, delay or cease development of other product candidates at any stage of pre-clinical or clinical development based on a variety of factors, including our judgments regarding costs or timing of further development, probability of success of clinical development, regulatory requirements, commercial potential, relative benefits and costs compared to other product candidates in our portfolio, and our overall corporate strategy. 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 discovery and product development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate 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

product candidate. Failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

We plan to evaluate CT-0525 in combination with pembrolizumab and may evaluate CT-0525 in combination with other drugs. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs, revoke their approval of such drugs, or if safety, efficacy, manufacturing or supply issues arise with the drugs we choose to evaluate in combination with CT-0525, we may be unable to obtain approval of CT-0525 or market CT-0525.

In November 2023, we received FDA clearance of our IND for CT-0525 and we expect to treat the first patient in the second quarter of 2024. We also plan to conduct a sub-study of our Phase 1 clinical trial utilizing CT-0525 in combination with pembrolizumab and may evaluate CT-0525 in combination with other drugs.

We did not develop or obtain marketing approval for, nor have we manufactured or sold, any of the currently approved drugs that we may study in combination with CT-0525. If the FDA or similar regulatory authorities outside of the United States revoke their approval of any drug or drugs in combination with which we determine to develop CT-0525, we will not be able to market CT-0525 in combination with such revoked drugs.

If safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays, and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate the applicable clinical trials. If the drugs we use are replaced as the standard of care for the indications we choose for CT-0525, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with CT-0525, we may not be able to complete clinical development of CT-0525 on our current timeline or at all.

Even if CT-0525 were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the drugs used in combination with CT-0525 or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our other product candidates for use in combination with other drugs for cancer or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially.

We may not be successful in our efforts to identify or discover additional potential product candidates.

A key element of our strategy is to apply our macrophage engineering platform to address a broad array of indications and targets to generate next-generation therapeutics, including three programs for indications outside of oncology. The discovery efforts that we are conducting may not be successful in identifying product candidates that are useful in treating cancer or other diseases. Our discovery engine may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance; or
- potential product candidates may not be effective in treating their targeted diseases.

Discovery programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify additional suitable product candidates for pre-clinical and clinical development, it will limit our potential to obtain revenues from sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Adverse public perception of genetic medicine, and gene therapy in particular, may negatively impact regulatory approval of, or demand for, our potential products.

The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will

depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates that we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Risks Related to the Commercialization of Our Product Candidates

Even if any of our product candidates receives marketing approval, we 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, and the market opportunity for any of our product candidates, if approved, may be smaller than we estimate.

If any of our product candidates receives marketing approval, we may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as chemotherapy and radiation therapy, are well established in the medical community and doctors may continue to rely on these and similar treatments. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from product sales and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our product candidates compared to the advantages and relative risks of alternative treatments;
- the effectiveness of sales and marketing efforts;
- our ability to offer our products, if approved, for sale at competitive prices;
- the clinical indications for which the product is approved;
- the cost of treatment in relation to alternative treatments;
- the 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 timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- product labeling or product insert requirements of the FDA, the European Medical Agency, or the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects;
- support from patient advocacy groups; and
- any restrictions on the use of our products, if approved, together with other medications.

Our assessment of the potential market opportunity for our product candidates is based on industry and market data that we obtained from industry publications, research, surveys and studies conducted by third parties and our analysis of these data, research, surveys and studies. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Our estimates of the potential market opportunities for our product candidates include a number of key assumptions based on our industry knowledge, industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for any of our product candidates may be smaller than we expect, and as a result our revenues from product sales may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience as a company in the sale, marketing or distribution of biopharmaceutical products. To achieve commercial success for any product for which we may obtain marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

We currently expect that we would build our own focused, specialized sales and marketing organization to support the commercialization in the United States of product candidates for which we receive marketing approval and that can be commercialized with such capabilities. There are risks involved with us establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a 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. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In general, the cost of establishing and maintaining a sales and marketing organization may exceed the cost-effectiveness of doing so.

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

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, market access, distribution, customer service, medical affairs and other support personnel;
- our inability to equip sales personnel with effective materials;
- our inability to effectively manage a geographically dispersed sales and marketing team;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- 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; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our revenues from product sales and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do, thus rendering our products non-competitive, obsolete or reducing the size of the market for our products.

The biopharmaceutical industry, and in particular the cell therapy field, is characterized by intense investment and competition aimed at rapidly advancing new technologies. Our platform and therapeutic product candidates are expected to face substantial competition from multiple technologies, marketed products and numerous other therapies being developed by third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition is likely to come from multiple sources, including biopharmaceutical companies, academic research institutions, governmental agencies and private research institutions that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. The competition is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research institutions.

We are aware of a number of companies generally pursuing the development of myeloid cell therapies, including, among others Myeloid Therapeutics, Shoreline Biosciences, Inceptor Bio, Thunder Bio, Resolution Therapeutics, CellOrigin, SIRPant Therapeutics, and others. We are also facing competition from companies pursuing autologous T cell therapies, allogeneic T cell therapies, NK and other cell therapies, direct *in vivo* reprogrammed cell therapies and other macrophage-targeted oncology therapeutics.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific 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 development 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. Our competitors also may obtain FDA or other marketing approval for their products more rapidly than we may obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

Technology in the biopharmaceutical industry has undergone rapid and significant change, and we expect that it will continue to do so. Any products or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development.

Mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific 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.

We have pursued and may in the future pursue the in-license or acquisition of rights to complementary technologies and product candidates on an opportunistic basis. However, we may be unable to in-license or acquire any additional technologies or product candidates from third parties. The acquisition and licensing of technologies and product candidates is a competitive area, and a number of more established companies also have similar strategies to in-license or acquire technologies and product candidates that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the relevant technology or product candidate on terms that would allow us to make an appropriate return on our investment.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we may obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also 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. The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products, including our product candidates. Government authorities and third-party payors, such as private health insurers and health

maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers its costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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. 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.

There can be no assurance that our product candidates, even if they are approved for sale in the United States, in the European Union or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the ongoing, planned and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such 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 ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of marketing approval, recall, restriction on the approval or a "black box" warning or contraindication for an approved drug;

- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy;
- distraction of management's attention from our primary business; and
- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may prevent or delay our ability to seek or obtain marketing approval for or commercialize our product candidates or otherwise harm our business. If we are not able to maintain these third-party relationships or if these arrangements are terminated, we may have to alter our development and commercialization plans and our business could be adversely affected.

We rely, and expect to continue to rely, on third-party clinical research organizations, in addition to other third parties such as research collaboratives, clinical data management organizations, medical institutions and clinical investigators, to conduct our Phase 1 clinical trial of CT-0525 and any other clinical trials we conduct. We currently have no plans to independently conduct clinical trials of our product candidates or any other product candidates that we may develop. These contract research organizations, or CROs, and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. These third-party arrangements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for discovery and product development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities in Europe and other jurisdictions have similar requirements. 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 are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash 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 concludes 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 marketing application we submit to the FDA. 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 more 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 can occur, which could materially impact our ability to meet our desired clinical development timelines. Although we plan to carefully manage our relationships with our CROs, investigators and other third parties, we may nonetheless encounter challenges or delays in the future, which could have a material and adverse impact on our business, financial condition and prospects.

We rely on third-party CMOs for the manufacture of both drug substance and finished drug product of our product candidates for pre-clinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third-party CMOs for both drug substance and finished drug product, as well as for commercial manufacture if any of our product candidates receive marketing approval. We also currently rely on these third parties for the manufacture of plasmid and viral vectors, patient leukapheresis material logistics, as well as packaging, labeling, sterilization, storage, distribution and other production logistics. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish any 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:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the potential failure to manufacture our product candidate or product according to our specifications;
- the potential failure to manufacture our product candidate or product according to our schedule or at all;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We or our third-party manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredients necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or active pharmaceutical ingredients, including shortages caused by the purchase of such raw materials or active pharmaceutical ingredients by our competitors or others. Our or our third-party manufacturers' failure to obtain the raw materials or active pharmaceutical ingredients necessary to manufacture sufficient quantities of our product candidates may have a material adverse effect on our business.

Our third-party manufacturers are subject to inspection and approval by regulatory authorities before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to ongoing inspection from time to time. Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If any of our current contract manufacturers cannot perform as agreed, we may be required to replace such

manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement or be unable to reach agreement with an alternative manufacturer.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

We anticipate seeking third-party collaborators for the research, development and commercialization of certain of our product candidates. For example, we entered into a strategic collaboration with Moderna in January 2022 focused on the development of *in vivo* CAR-M therapeutics for up to twelve product candidates. In collaboration with Moderna, we have established a mRNA/LNP *in vivo* CAR-M platform for oncology targets, which enables an off-the-shelf approach wherein the patient's own myeloid cells are engineered directly within their body via the administration of a LNP encapsulating macrophage reprogramming mRNA CAR constructs, removing the requirement for *ex vivo* cell manufacturing entirely.

Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies and biotechnology companies.

Any such arrangements with third parties will likely limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts 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 discovery programs or any product candidates we may develop, including our collaboration with Moderna, pose the following risks to us:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations; for example, our collaboration with Moderna is managed by a joint steering committee, or JSC, which is comprised of representatives from the company and Moderna, with Moderna having final decision-making authority, subject to specified limitations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition or business combination, that divert resources or create competing priorities;
- collaborators may not pursue development and commercialization of any product candidates that achieve marketing approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition or business combination, that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, 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;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis; for example, data, results and know-how generated in the performance of the Moderna collaboration is deemed the confidential information of Moderna, which we may not disclose except under limited circumstances;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator may seek to renegotiate or terminate their relationship with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve marketing approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation; for example, Moderna has the first right to prosecute, enforce or defend certain patent rights under its agreement with us, and although we may have the right to assume the prosecution, enforcement or defense of such patent rights if Moderna does not, our ability to do so may be compromised by Moderna's actions;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability;
- collaborations may be terminated, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates; for example, Moderna has the right to terminate its agreement with us for convenience in its entirety or with respect to a specific product or target on ninety days' prior notice, in connection with a material breach of the agreement by us that remains uncured for a specified period of time or in the event of specified insolvency events involving us; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If a present or future collaborator of ours was to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, or receive it in the timeframe in which we expect to receive it, the development of our product candidates could be delayed, and we may need additional resources to develop our product candidates. All of the risks relating to product development, marketing approval and commercialization described herein also apply to the activities of our collaborators.

We may in the future decide to collaborate with biopharmaceutical companies for the development and potential commercialization of any product candidates we may develop. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

We may seek to establish additional collaborations. If we are not able to establish or maintain additional collaborations, on commercially reasonable terms, we may have to alter our development and commercialization plans and our business could be adversely affected.

To realize the full potential of our macrophage engineering platform and accelerate the development of additional macrophage engineering programs, we plan to continue to selectively pursue collaborations with leading biopharmaceutical companies with particular experience, including development and commercial expertise and capabilities. We face significant competition in attracting appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial 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. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate, document and execute. In addition, there have been a significant number of recent business combinations among large biopharmaceutical companies that have resulted in a reduced number of potential future collaborators. Any collaboration we may enter into may limit our ability to enter into future agreements on particular terms or covering similar target indications with other potential collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay our development program or one or more of our other development programs, delay our 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and generate revenue from product sales, which could have an adverse effect on our business, prospects, financial condition and results of operations.

We have a number of academic collaborations to supplement our internal discovery and product development programs. If any such collaborator decides to discontinue or devote less resources to such research, our discovery programs could be diminished.

Our discovery engine is supplemented by academic collaborations to expand our platform, which we rely upon to advance our development and commercialization plans for our product candidates. In August 2020, we entered into a scientific research and licensing agreement with Nathaniel R. Landau, Ph.D. and NYU Langone Health through which we obtained exclusive rights to develop their Vpx lentiviral vector globally for all indications. We also have an ongoing discovery program in neurodegeneration being pursued through a sponsored research agreement with Dr. Saar Gill, Associate Professor of Medicine at the University of Pennsylvania and co-founder of our Company, to develop CAR macrophages and microglia targeted against protein aggregates associated with neurodegenerative disease pathology. In addition, we, from time to time, may enter into academic research collaborations to explore the development of new technologies and indications.

While these academic institutions have contractual obligations to us, they are independent entities and are not under our control or the control of our officers or directors. Our research and licensing agreements with academic collaborators generally provide academic collaborators with license maintenance fees, development and regulatory milestone payments, royalties on net sales of products and a portion of sublicense income that we receive. Upon the scheduled expiration of any academic collaboration, we may not be able to renew the related agreement, or any renewal could be on terms less favorable to us than those contained in the existing agreement. Furthermore, either we or the academic institution generally may terminate the sponsored research agreement for convenience following a specified notice period. If any of these

academic institutions decides to not renew or to terminate the related agreement or decides to devote fewer resources to such activities, our discovery efforts would be diminished, while our royalty obligations, if any, would continue unmodified.

Any acquisitions or in-license transactions that we complete could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

We have licensed three patent families from Penn and one patent family from NYU and may enter into transactions to in-license or acquire other businesses, intellectual property, technologies, product candidates or products. If we determine to pursue a particular transaction, we may not be able to complete the transaction on favorable terms, or at all. Any in-licenses or acquisitions we complete may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an in-license or acquisition or issue our common stock or other equity securities to the stockholders of the target company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. In-license and acquisition transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of additional future in-licenses or acquisitions or the effect that any such transactions might have on our operating results.

The FDA, European Medicines Agency, or EMA, or other comparable foreign regulatory authorities could require the clearance or approval of a companion diagnostic device as a condition of approval for any product candidate that requires or would commercially benefit from such tests. Failure to successfully validate, develop and obtain regulatory clearance or approval for companion diagnostics on a timely basis or at all could harm our product development strategy and we may not realize the commercial potential of any such product candidate.

If safe and effective use of any of our other product candidates depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates. The process of obtaining or creating such diagnostic is time consuming and costly. Companion diagnostics, which provide information that is essential for the safe and effective use of a corresponding therapeutic product, are subject to regulation by the FDA, EMA and other comparable foreign regulatory authorities as medical devices and require separate regulatory approval from therapeutic approval prior to commercialization. The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of pre-clinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Given our limited experience in developing and commercializing diagnostics, we do not plan to develop companion diagnostics internally and thus will be dependent on the sustained cooperation and effort of third-party collaborators in developing and obtaining approval for these companion diagnostics. We may not be able to enter into arrangements with a provider to develop a companion diagnostic for use in connection with a registrational trial for our product candidates or for commercialization of our product candidates, or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, we, our collaborators or third parties may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics by physicians.

Any companion diagnostic collaborator or third party with whom we contract may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates, or our relationship with such collaborator or third party may otherwise terminate. We may not be able to enter into arrangements with another provider to obtain supplies of an alternative

diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

Risks Related to Our Intellectual Property

If we are unable to obtain, maintain and enforce patent protection for our technology and product candidates or if the scope of the patent 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 and we may not be able to compete effectively in our market.

Our commercial success depends in part on our ability to obtain, maintain and enforce protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business and by in-licensing intellectual property related to such technologies and product candidates. If we are unable to obtain, maintain or enforce patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co-own or license may fail to result in issued patents in the United States or in other foreign countries.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. 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, or in some cases not published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Moreover, our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our technology and product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. If the breadth or strength of

protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Our owned or licensed patent estate includes patent applications, many of which are at an early stage of prosecution. The coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned or in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to our inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, 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 costs and require significant time from our management and employees, even if the eventual outcome is favorable to us. 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. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position with respect to our current or future product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but there is no assurance that any such extensions will be obtained, and the life of a patent, and the protection it affords, is limited. Even if patents covering our current or future product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

In the United States, patent term can also be adjusted due to delays that occur during examination of patent applications, which may extend the term of a patent beyond 20 years. There is a risk that we may take action that detracts from any accrued patent term adjustment.

It is necessary to pay certain maintenance fees, also referred to as annuities or renewal fees in some countries, throughout the lifetime of a patent at regular intervals. Failure to pay these fees can cause a granted patent to prematurely expire, without an opportunity for revival. There is a risk that we may be unable to maintain patent protection for certain patents in all markets due to finite availability of resources.

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

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. 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, we may be unable to develop or commercialize the affected product candidate(s), which could materially harm our business and the third parties owning 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, we may be non-exclusive, thereby giving our competitors access to the same technologies licensed 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 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 us having to negotiate new or restated 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.

If we do not obtain patent term extension for any product candidates we may develop, our business may be materially harmed.

In the United States, the term of a patent that covers an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Hatch-Waxman Act, as compensation for the loss of a patent term during the FDA regulatory review process for a drug product subject to the provisions of the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years, but patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. There is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions could be for a shorter period than we anticipate. We may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the maintenance, enforcement or defense of our owned or in-licensed issued patents.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future.

The federal government retains certain rights in inventions created using 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 the patent owner refuses to do so, the government may grant the license itself. We collaborate with a number of universities with respect to certain of our research and development. We cannot be sure that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or in-license technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

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

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our licensor's issued patents, the patents of our licensors or other intellectual property. It may be difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's product. To counter infringement or misappropriation, we or our licensors may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming and can distract our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Any claims we assert against perceived infringers could provoke such 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 or our licensors have asserted are invalid or unenforceable. 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 novelty, non-obviousness, enablement, or written description. 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, such as opposition proceedings. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Similarly, if we or our licensors assert trademark infringement claims, a court may determine that the marks we or our licensors have asserted are invalid or unenforceable, or that the party against whom we or our licensors 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.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated, held unenforceable or interpreted narrowly, could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent, and could limit our or our licensor's ability to assert those patents against those parties, or other competitors, and curtail or preclude our ability to exclude third parties from developing and commercializing similar or competitive products. A court may also refuse to stop the third party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. Even if we establish infringement, a court may not order the third party to stop using the technology at issue and instead award only monetary damages to us, which 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 or trade secrets 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 allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our

management, technical personnel and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Any such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources in one or more aspects, or for other reasons. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or products, in which case we would be required to obtain a license from such third party. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than us, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the biopharmaceutical industry. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions, such as opposition proceedings before the European Patent Office. 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. As the biopharmaceutical industry expands and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so 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 substantially 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 merit. Even if we diligently search third-party patents for potential infringement by our products or product candidates, we may not successfully find patents our products or product candidates may infringe. We may not be aware of all such 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 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.

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 materials, formulations or methods, such as methods of manufacture or methods for treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringe upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, 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, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. 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 or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could also be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we are able to obtain a license, we could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right, we could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

While we seek to protect the trademarks and trade names we use in the United States and in other countries, we may be unsuccessful in obtaining registrations or otherwise protecting these trademarks and trade names, which we need to build name recognition in our markets of interest and among potential partners or customers. We rely on both registration and common law protection for our trademarks. Our registered or unregistered trademarks or trade names may be challenged, infringed, diluted or declared generic, or determined to be infringing on other marks. At times, competitors may adopt trademarks and trade names similar to ours, or our collaborators may fail to use our trade names or trademarks, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks. If we are unable to protect our rights to trademarks and trade names, we may be prevented from using such marks and names unless we enter into appropriate royalty, license or coexistence agreements, which may not be available or may not be available on commercially reasonable terms.

During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Effective trademark protection may not be available or may not be

sought in every country in which our products are made available. Any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be adversely affected.

We may license our trademarks and trade names to third parties, such as distributors and collaborators. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of or failure to use our trademarks and trade names by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, know-how, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining 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.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our current and future intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to a number of license and research agreements. Some of these agreements provide us with the intellectual property rights required for the development of our product candidates, including the license agreement with Penn. These

licenses and research agreements and similar agreements in the future may impose diligence, development and commercialization timelines, and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with such obligations, the parties to these agreements may decide to terminate the agreements or require us to grant them certain rights, in which we may not be able to develop, manufacture, or market any products without the rights granted to us by these agreements and may face other penalties. Any such occurrences could adversely affect the value of any product candidate being developed, including CT-0525.

For a variety of purposes, we will likely enter into additional licensing and funding arrangements with third parties that may impose similar obligations on us. Termination of these agreements or reduction or elimination of our rights under these agreements may result in us having to negotiate new or restated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects. While we still face all of the risks described herein with respect to such agreements, we cannot prevent third parties from also accessing those technologies. In addition, our licenses may place restrictions on our future business opportunities.

In addition to the above risks, intellectual property rights that our licenses in the future may include sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the payment obligations with respect to licensed technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Further, licensors could retain the right to prosecute and defend the intellectual property rights licensed to us, in which case we would depend on our licensors to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and upstream licensors, which may not be forthcoming. Licensors may determine not to pursue litigation against other companies or may pursue such litigation less aggressively than we would. Our business could be adversely affected if we or our licensors are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications of our in-licenses. If other third parties have ownership rights to patents or patent applications of our in-licenses, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product

candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive. 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, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may 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 or licenses, but enforcement is not as strong as that in the United States. 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.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many 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 with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, including of their current or former employers or claims asserting we have misappropriated their intellectual property, or is claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors have been previously employed at universities or other biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We may have also entered into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. To the extent we become involved in litigation that may require discovery of our trade secrets, know-how and other proprietary technology, we will seek to secure protective orders from the court that bind the parties with access to the discovered information. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and 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 of the United States are less willing or unwilling to protect trade secrets. In addition, we cannot be certain that proprietary technical information and related confidential documents that we have shared with our collaborators and/or submitted to governmental agencies, including regulatory agencies for evaluation and supervision of pharmaceutical products, will be kept confidential. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats to us.

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. For example:

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own or license;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering our inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned or in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- claims of issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research, development, testing or commercialization activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- the U.S. Supreme Court, other 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 or our licensors' patents;
- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- 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.

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

If approved, our product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic.

Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product In addition, the licensure 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 develop and receive approval of a competing biologic, so long as its BLA does not reply on the reference product, sponsor's data or submit the application as a biosimilar application.

We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12-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 the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the 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. Nonetheless, the approval of a biosimilar to our product candidates would have a material adverse impact on our business due to increased competition and pricing pressure.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval process of the FDA is lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA 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 marketing approval for any product candidate and it is possible that none of our existing product candidates, or any product candidates we may seek to develop in the future will ever obtain marketing approval.

Our product candidates could fail to receive marketing approval for many reasons, including the following:

- the FDA may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA that a product candidate is safe and effective for our proposed indication;
- results of clinical trials may not meet the level of statistical significance required by the FDA for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- data collected from clinical trials of our product candidates may not be sufficient to support the submission of a new drug application, or NDA, to the FDA or other submission or to obtain marketing approval in the United States;
- the FDA may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in us failing to obtain marketing approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. The FDA has substantial discretion in the approval process and determining when or whether marketing approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA. Risks similar to those outlined above exist with regard to regulatory authorities outside the United States.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we complete the necessary pre-clinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by the EMA and other regulatory authorities outside of the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive pre-clinical and clinical data and supporting

information, including manufacturing information, to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude us from obtaining marketing approval or prevent or limit commercial use. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional pre-clinical, clinical or other studies. In addition, varying interpretations of the data obtained from pre-clinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Further, under the PREA, a BLA or supplement to a BLA for certain biological products must contain data to assess the safety and effectiveness of the biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the European Union also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and EU Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, became responsible for supervising medicines and medical devices in Great Britain, or GB, comprising England, Scotland and Wales under domestic law, whereas under the terms of the Northern Ireland Protocol, Northern Ireland is currently subject to EU rules. The United Kingdom and European Union have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the United Kingdom. Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products

destined for the United Kingdom, or UK, market (i.e., GB and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. Any delay in obtaining, or an inability to obtain, any marketing authorizations, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Inadequate funding for the FDA, the Securities and Exchange Commission, or the SEC, and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the FDA have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, EMA and other agencies 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, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

Accordingly, if a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Regulatory requirements governing gene therapy products are periodically updated and may continue to change in the future.

The FDA has established the OTAT, within the Center for Biologics Evaluation and Research, or the CBER, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. In September 2022, the FDA announced retitling of the OTAT to the OTP, and

elevation of the OTP to a "Super Office" to meet its growing cell and gene therapy workload and new commitments under the Prescription Drug User Fee Act agreement for fiscal years 2023 to 2027.

Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH also are potentially subject to review by the Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RDAC; however, the NIH announced that the RDAC will only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks. Although the FDA decides whether individual gene therapy protocols may proceed, the RDAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on a clinical hold even if the RDAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's Institutional Biosafety Committee, or IBC, as well as our IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of our product candidates.

The FDA has issued various guidance documents regarding gene therapies, including final guidance documents released in January 2020 relating to CMC information for gene therapy INDs, gene therapies for rare diseases and gene therapies for retinal disorders. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any gene therapy product candidate that we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper pre-clinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND; the proper design of tests to measure product potency in support of an IND or BLA; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

Further, for a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with GTP. These standards are found in FDA regulations and guidance that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Finally, ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations or prohibiting the processes that we may use. Federal and state agencies, congressional committees and foreign governments have expressed their intentions to further regulate biotechnology. More restrictive regulations or claims that our product candidates are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

As we advance our product candidates through clinical development, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, 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. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue.

Any product for which we obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with any such product following approval.

Any product for which we obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing

requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market any product for an indication that is not approved, we may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with any product for which we may obtain marketing approval and its manufacturers or manufacturing processes or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such product, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of the product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of the product;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of the product;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Finally, our ability to develop and market new drug products may be impacted by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the United States. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA's drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug.

On April 12, 2023, the district court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U.S. Supreme Court entered a stay of the district court's decision, in its entirety, pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to or the Supreme Court. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023, and, on August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market, finding that a challenge to the FDA's initial approval in 2000 is barred by the statute of limitations. But the Appeals Court did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that

asked the U.S. Supreme Court to review the Appeals Court decision. On December 13, 2023, the Supreme Court granted these petitions for writ of certiorari for the appeals court decision.

Similar restrictions apply to the approval of our products in the EU. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to EU Member State laws. The failure to comply with these and other EU requirements can also lead to significant penalties and sanctions.

Any regulatory approval to market our products will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Physicians may nevertheless prescribe our products off-label to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our products for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the PIE Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the HHS, the FDA, the Federal Trade Commission, or the FTC, and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "*qui tam*" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a *qui tam* suit is entitled to a share of any recovery or settlement. *Qui tam* suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a *qui tam* suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate

integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the United States, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We may seek PRIME Designation in the European Union for our product candidates, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

In the EU, we may seek PRIME designation for some of our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the European Union or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the European Union and where the sponsor intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

We, or our collaborators, may seek approval from the FDA or comparable foreign regulatory authorities to use accelerated development pathways for our product candidates. If we, or our collaborators, are not able to use such pathways, we, or they, may be required to conduct additional clinical trials beyond those that are contemplated, which would increase the expense of obtaining, and delay the receipt of, necessary marketing approvals, if we, or they, receive them at all. In addition, even if an accelerated approval pathway is available to us, or our collaborators, it may not lead to expedited approval of our product candidates, or approval at all.

Under the Federal Food, Drug, and Cosmetic Act and implementing regulations, the FDA may grant accelerated approval to a product candidate to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies, upon a determination that the product has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. Prior to seeking such accelerated approval, we, or our collaborators, will continue to seek feedback from the FDA or comparable foreign regulatory agencies and otherwise evaluate our, or their, ability to seek and receive such accelerated approval.

With passage of the FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to the FDA every six months (until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, the FDORA requires the FDA to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

More recently, in March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and will not be legally binding even when finalized, we will need to consider the FDA's guidance closely if we seek accelerated approval for any of our products.

There can be no assurance that the FDA or comparable foreign regulatory agencies will agree with our, or our collaborators', surrogate endpoints or intermediate clinical endpoints in any of our, or their, clinical trials, or that we, or our collaborators, will decide to pursue or submit any additional application for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from the FDA or comparable foreign regulatory agencies, we, or our collaborators, will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval. Furthermore, for any submission of an application for accelerated approval or application under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted for filing or that any expedited development, review or approval will be granted on a timely basis, or at all.

A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period until commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may not be able to obtain orphan drug exclusivity for any product candidates we may develop, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the FDA must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA and comparable foreign regulatory authorities such as the EMA can subsequently approve the same product for the same condition if the FDA or such other authorities conclude that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

In 2017, the Congress passed the FDARA. The FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. Under omnibus legislation signed by former President Trump in December 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of the FDARA in 2017, but have not yet been approved or licensed by the FDA.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

If we are required by the FDA, EMA or comparable regulatory authority to obtain clearance or approval of a companion diagnostic test in connection with approval of any of our product candidates or a group of therapeutic products, and we do not obtain or we face delays in obtaining clearance or approval of a diagnostic test, we may not be able to commercialize the product candidate and our ability to generate revenue may be materially impaired.

If we are required by the FDA, EMA or a comparable regulatory authority to obtain clearance or approval of a companion diagnostic test in connection with approval of any of our product candidates, such companion diagnostic test would be used during our more advanced phase clinical trials as well as in connection with the commercialization of our product candidates. To be successful in developing and commercializing product candidates in combination with these companion diagnostics, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to ensuring the safe and effective use of a novel therapeutic product or new indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared. In

certain circumstances (for example, when a therapeutic product is intended to treat a serious or life-threatening condition for which no satisfactory available therapy exists or when the labelling of an approved product needs to be revised to address a serious safety issue), however, the FDA may approve a therapeutic product without the prior or contemporaneous marketing authorization of a companion diagnostic. In this case, approval of a companion diagnostic may be a post-marketing requirement or commitment.

Co-development of companion diagnostics and therapeutic products is critical to the advancement of precision medicine. Whether initiated at the outset of development or at a later point, co-development should generally be conducted in a way that will facilitate obtaining contemporaneous marketing authorizations for the therapeutic product and the associated companion diagnostic. If a companion diagnostic is required to identify patients who are most likely to benefit from receiving the product, to be at increased risk for serious adverse events as a result of treatment with a particular therapeutic product, or to monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness, then the FDA has required marketing approval of all companion diagnostic tests essential for the safe and effective use of a therapeutic product for cancer therapies. Various foreign regulatory authorities also regulate in vitro companion diagnostics as medical devices and, under those regulatory frameworks, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any future diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization in those countries.

The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genomic alteration or mutation alteration that the companion diagnostic was developed to detect. If the FDA, EMA or a comparable regulatory authority requires clearance or approval of a companion diagnostic for any of our product candidates, whether before, concurrently with approval, or post-approval of the product candidate, we, and/or future collaborators, may encounter difficulties in developing and obtaining clearance or approval for these companion diagnostics. The process of obtaining or creating such companion diagnostics is time consuming and costly. The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain PMA, simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of pre-clinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the sponsor must prepare and provide FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Any delay or failure by us or third-party collaborators to develop or obtain regulatory clearance or approval of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates. Further, in April 2020, the FDA issued new guidance on developing and labeling companion diagnostics for a specific group of oncology therapeutic products, including recommendations to support a broader labeling claim rather than individual therapeutic products. We will continue to evaluate the impact of this guidance on our companion diagnostic development and strategy. This guidance and future issuances from the FDA, EMA and other regulatory authorities may impact our development of a companion diagnostic for our product candidates and could result in delays in regulatory clearance or approval or a change in the determination for whether or not a companion diagnostic is still required for our product candidates. We may be required to conduct additional studies to support a broader claim or more narrowed claim for a subset population. Also, to the extent other approved diagnostics are able to broaden their labeling claims to include any of our future approved product candidates covered indications, we may no longer need to continue our companion diagnostic development plans or we may need to alter those companion diagnostic development strategies, which could adversely impact our ability to generate revenue from the sale of our companion diagnostic test.

Additionally, we may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining clearance or approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory clearance or approval processes. Moreover, even if data from pre-clinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance or approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance.

If we are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of our product candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the co-development or commercialization of our companion diagnostic and therapeutic product candidates.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to civil, criminal and administrative sanctions, contractual damages, reputational harm and diminished future profits and earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable state and federal fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

- *Anti-Kickback Statute* - prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, ordering, leasing, arranging for, or recommending the purchasing, ordering, or leasing of, any good or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare or Medicaid;
- *False Claims Act* - the federal civil and criminal false claims laws, including the civil False Claims Act, and Civil Monetary Penalties Law, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or knowingly making, using or causing to made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government;
- *HIPAA* - the federal HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and apply regardless of the payor (e.g., public or private);
- *HIPAA and HITECH* - HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose obligations on HIPAA covered entities and their business associates, including mandatory contractual terms and required implementation of administrative, physical and technical safeguards to maintain the privacy and security of individually identifiable health information;
- *Transparency Requirements* - the federal physician transparency requirements known as the Physician Payments Sunshine Act, under the ACA, as amended by the Health Care Education Reconciliation Act, which requires manufacturers of drugs, medical devices, biological and medical supplies covered by Medicare, Medicaid, or State Children's Health Insurance Program to report annually to the CMS, within the HHS information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- *Analogous State, Local and Foreign Laws* - analogous state, local and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader than similar federal laws, can apply to claims involving healthcare items or services regardless of payor, and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, as well as tracking and reporting of transfers of value by pharmaceutical manufacturers to physicians and

healthcare organizations, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and/or administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States.

Current and future legislation may increase the difficulty and cost for us and any of our collaborators to obtain marketing approval of and commercialize product candidates and affect the prices we, or any of our collaborators, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, impact pricing and reimbursement and affect our ability, or the ability of any of our collaborators, to profitably sell or commercialize any product candidates for which we, or any of our collaborators, obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. 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. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any of our collaborators, may receive for any FDA approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for prescription drugs purchased through a pharmacy by the elderly and disabled and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this statute provides authority for limiting the number of drugs that will be covered in any therapeutic class, subject to certain exceptions. Cost reduction initiatives and other provisions of this statute could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, then-President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Under current legislation, the actual reductions in Medicare payments may vary up to 4%.

The Consolidated Appropriations Act, or the Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Appropriation Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Further, with passage of the IRA, Congress extended the expansion of the Patient Protection and Affordable Care Act premium tax credits through 2025. Those subsidies were originally extended through 2022 under the American Rescue Plan Act of 2021. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, in June 2021, the U.S. Supreme Court dismissed a lawsuit challenging the constitutionality of the ACA after finding that the plaintiffs do not have standing to bring the litigation. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the health insurance marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This executive order also directs the HHS to create a special enrollment period for the health insurance marketplace in response to the COVID-19 pandemic.

In the EU, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to scrutiny and considerable legislative and executive actions that could impact the prices we obtain for our drug products, if and when approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States and foreign jurisdictions. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, former President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the CMS issued a final rule to rescind it. With issuance of this rule, the CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the PhRMA but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation.

Further, on November 20, 2020, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The IRA further delayed implementation of this rule to January 1, 2032.

On August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. 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 HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs

at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, or the Chamber, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing 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. In addition, health care organizations 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In other countries, particularly the countries of the European Union, 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, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the FCPA the Bribery Act, and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act, or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, United Kingdom, and authorities in the European Union, including

applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which is collectively referred to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements, including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have a material adverse impact on our business, financial condition, results of operations and liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control Laws by the United States, the United Kingdom or other authorities could also have an adverse impact on our reputation, business, results of operations and financial condition.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States, the European Union and the United Kingdom. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in an enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. The HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In addition to potential enforcement by the HHS, we are also potentially subject to privacy enforcement from the FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

States are also active in creating specific rules relating to the processing of personal information. In 2018, California passed into law the CCPA which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the CPRA, which will significantly expand the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. Most CPRA provisions took effect on January 1, 2023, though the obligations apply to any personal information collected after January 1, 2022. These provisions may apply to some of our business activities.

In addition to California, eleven other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Similar to the laws in the United States, there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or the EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20.0 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the European Union to countries that have not been found by the European Commission to offer adequate data protection legislation, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the European Union to other countries. In July 2020, the Court of Justice of the EU, or the CJEU, invalidated the European Union-United States Privacy Shield, or Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. While we are not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the United States, generally, and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Following the CJEU decision, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission adopted the adequacy decision in July 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be

challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business.

On June 23, 2016, the electorate in the United Kingdom. voted in favor of leaving the European Union, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the United Kingdom. and whether personal information can transfer from the European Union to the United Kingdom. Following the withdrawal of the United Kingdom from the European Union, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under the GDPR, although these transfers currently are permitted by an adequacy decision from the European Commission. The UK government has already determined that it considers all European Union 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom. to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the United Kingdom. as being "essentially adequate" for purposes of data transfer from the European Union to the United Kingdom., although this decision may be re-evaluated in the future. The United Kingdom. and the United States. have also agreed to a U.S.-UK "Data Bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the United Kingdom to the United States. In addition to the United Kingdom., Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

If our employees, independent contractors, consultants, collaborators and vendors engage in misconduct or other improper activities, including non-compliance with regulatory standards and/or requirements and insider trading, we could sustain significant liability and harm to our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, collaborators and vendors. Misconduct by these partners could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of foreign jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee or

third-party misconduct, and the precautions that we take to detect and prevent these activities 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 be in compliance with such laws, standards, regulations, guidance or codes of conduct. 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 fines or other sanctions.

If we or any third-party manufacturer we engage now or in the future fails to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could significantly harm our business.

We and third-party manufacturers we engage now are, and any third-party manufacturer we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Although we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain general liability insurance as well as workers' compensation insurance to cover costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

Our reduction in force undertaken to extend our cash runway and focus more of our capital resources on our prioritized research and development programs might not achieve our intended outcome.

In late March 2024, our board of directors approved a reduction in force affecting approximately 37% of our total workforce, in order to preserve cash and prioritize investment in our core clinical programs. The reduction in force may result in unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond the intended number of employees, decreased morale among our remaining employees, and the risk that we may not achieve the anticipated benefits of the reduction in force. In addition, while positions have been eliminated, certain functions necessary to our operations remain, and we might not successfully distribute the duties and obligations of our terminated employees among our remaining employees. The reduction in workforce could also make it difficult for us to pursue, or prevent us from pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. If we are unable to realize the anticipated benefits from the reduction in force, or if we experience significant adverse consequences from the reduction in force, our business, financial condition and results of operations may be materially adversely affected.

Our future success depends on our ability to retain key executives and experienced scientists and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we entered into employment agreements with certain of our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel is also critical to our success.

The loss of the services of our executive officers or other key employees, including temporary loss due to illness, could impede the achievement of our discovery programs, development and commercialization objectives and seriously harm our

ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult 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 successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous biopharmaceutical companies for similar personnel. We also experience competition for the hiring of 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 discovery, research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Failure to succeed in clinical trials may make it even more challenging to recruit and retain qualified scientific personnel. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly as we function as a public company and in the areas of product development, clinical, regulatory affairs, manufacturing and quality control and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Future growth will impose significant added responsibilities on members of our management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and regulatory review process for CT-0525 and other product candidates we are developing or may develop in the future, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to advance development of and, if approved, commercialize CT-0525 and any other product candidate we are developing or may develop in the future will depend, in part, on our ability to effectively manage any future growth. 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. If we do not effectively manage the expansion of our operations, we could experience weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations could also lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Many of the biopharmaceutical companies, and in particular cell therapy 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. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can develop product candidates and operate our business will be limited.

Our internal computer systems, or those of our collaborators, vendors, suppliers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any of our collaborators, vendors, suppliers, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the

confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or email fraud to cause payments or information to be transmitted to an unintended recipient.

If we experience any material system failure, accident, cyber-attack or security that causes interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our marketing 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 confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

Our employees, independent contractors, including principal investigators, consultants and vendors and any third parties we may engage in connection with discovery programs, research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, including principal investigators, consultants and vendors and any other third parties we engage. Misconduct by these parties could include intentional, reckless or negligent conduct or unauthorized activities that include failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide complete and accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state data privacy, security, fraud and other healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report complete financial information or data accurately or disclose unauthorized activities to us. Misconduct by employees and other third parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the EU Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. 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 be in compliance with such laws, standards, regulations, guidance or codes of conduct. Additionally, we are subject to the risk that a person 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.

Risks Related to the Ownership of Our Common Stock

The market price of our common stock may be volatile, and the market price of our common stock may drop in the future.

The market price of our common stock could be subject to significant fluctuations. Some of the factors that may cause the market price of our common stock to fluctuate include:

- results of clinical trials and pre-clinical studies of our product candidates, or those of our competitors or our existing or future collaborators;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- actions taken by regulatory agencies with respect to our product candidates, clinical studies, manufacturing process or sales and marketing terms;

- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of qualified scientific and management personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue adverse or misleading opinions regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions or market conditions in the biopharmaceutical sector;
- sales of securities by us or our stockholders in the future;
- if we fail to raise an adequate amount of capital to fund our operations and continued development of our product candidates;
- trading volume of our common stock;
- announcements by competitors of new commercial products, clinical progress or lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to product candidates, including with respect to other products in such markets;
- the introduction of technological innovations or new therapies that compete with our products and services; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. In addition, a recession, depression or other sustained adverse market event could materially and adversely affect our business and the value of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against such companies. Furthermore, market volatility may lead to increased shareholder activism if we experience a market valuation that activists believe is not reflective of its intrinsic value. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition.

We incur additional costs and increased demands upon management as a result of complying with the laws and regulations affecting public companies.

We incur significant legal, accounting and other expenses as a public company that we did not incur as a private company, including costs associated with public company reporting obligations under the Exchange Act. Some of our management team has not previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise related to public company reporting requirements and compliance with applicable laws and regulations to ensure that we comply with all of these requirements. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on the board of directors or on board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could 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. Certain of our stockholders have rights, subject to specified conditions, under our resale registration statement on Form S-3 registering 3,730,608 shares of our common stock under which they may sell their shares of common stock in the public market, so long as the resale registration statement on Form S-3 remains effective. We have also filed a registration statement registering all shares of common stock that we may issue under our equity compensation plans.

Moreover, we are also party to the Sale Agreement with Jefferies, as sales agent, pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $100.0 million from time to time through Jefferies under an "at-the-market offering" program, or ATM. The number of shares that are sold by Jefferies after we request that sales be made will fluctuate based on the market price of our common stock during the sales period and limits we set with Jefferies. Therefore, it is not possible to predict the number of shares that will ultimately be issued by us, if any, pursuant to

the sales agreement. As of December 31, 2023, we have sold 226,533 shares under the ATM for gross proceeds of $0.6 million. From January through March 2024, the Company sold an additional 931,250 shares under the ATM for gross proceeds of $2.4 million.

If at some point we are no longer a "smaller reporting company" or otherwise no longer qualify for applicable exemptions, we will be subject to additional laws and regulations affecting public companies that will increase our costs and the demands on management and could harm our operating results.

We will be subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition as well as other disclosure and corporate governance requirements. However, as a "smaller reporting company," as defined in Item 10(f)(1) of Regulation S-K, we may take advantage of certain exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2022 and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. If at some point we are no longer qualified as a smaller reporting company or otherwise no longer qualify for these exemptions, we will be required to comply with these additional legal and regulatory requirements applicable to public companies and will incur significant legal, accounting and other expenses to do so. If we are not able to comply with the requirements in a timely manner or at all, our financial condition or the market price of our common stock may be harmed. For example, if we or our independent auditor identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, then we could face additional costs to remedy those deficiencies, the market price of our stock could decline or we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

Our executive officers, directors and principal stockholders may have the ability to significantly influence all matters submitted to our stockholders for approval.

As of December 31, 2023, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned 47.7% of our outstanding shares of common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of the company on terms that other stockholders may desire.

We have broad discretion in the use of our cash and cash equivalents and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

We have broad discretion over the use of our cash and cash equivalents. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Our failure to apply these resources effectively could compromise our ability to pursue our growth strategy and we may not be able to yield a significant return, if any, on our investment of these net proceeds. You do not have the opportunity to influence our decisions on how to use our cash resources.

We are in the process of unwinding contractual relationships related to a strategic transaction with respect to Vicineum, which may adversely impact our business, financial condition and results of operations.

On July 15, 2022, Sesen Bio made the strategic decision to voluntarily pause further development of Vicineum in the United States. and we do not expect to pursue further development of Vicineum for the treatment of non-muscle invasive bladder cancer. Sesen Bio previously entered into various agreements and licenses with licensees, licensors and other counterparties related to the development and/or commercialization of Vicineum. Prior to the consummation of the Merger of the company and Sesen Bio, Sesen Bio began the process of winding down its operations relating to Vicineum. The process of unwinding contractual relationships related to Vicineum is ongoing, and may divert the attention of our management team and employees from day-to-day business, result in liability, impose additional costs and otherwise adversely affect our business and financial condition.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

We have established processes for assessing, identifying and managing cybersecurity risks, which are built into our overall risk management program and are designed to help protect our information assets and operations from internal and external cyber threats, protect employee and patient information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural and technical safeguards. We engage certain third parties to enhance and assist with our cybersecurity oversight, including a 24/7 Security Operation Center, or SOC, that monitors network devices and computer systems in real time. We include confidentiality and data protection provisions in certain contracts with third-party service providers to help protect us and our patients from any related vulnerabilities.

We do not believe that there are currently any known risks from cybersecurity threats that have or are reasonably likely to materially affect us or our business strategy, results of operations or financial condition. However, despite our efforts, we cannot eliminate all risks from cybersecurity threats, or provide assurances that we have not experienced undetected cybersecurity incidents. For more information on the most pertinent risks we may experience from cybersecurity threats, please refer to Part I, Item 1A, "Risk Factors" – "*Our internal computer systems, or those of our collaborators, vendors, suppliers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs*."

Cybersecurity Governance and Oversight

The audit committee of our board of directors provides oversight over cybersecurity risk and updates the full board of directors periodically regarding such oversight. The audit committee reviews and discusses with management the Company's major risk exposures, including cybersecurity matters, and is notified between such updates regarding significant new cybersecurity threats or incidents, if any.

Our General Counsel leads the operational oversight of company-wide cybersecurity strategy, policy, standards and processes and works across relevant departments to assess and help prepare us and our employees to address cybersecurity risks. The consultant that operates our SOC updates the General Counsel regarding the detection of cybersecurity risk exposure and provides advice on the prevention, mitigation and remediation of such risks. The General Counsel keeps the senior executive leadership team apprised, including our Chief Executive Officer and Chief Financial Officer, on assessments of risk exposure to ensure that the highest levels of management are kept abreast of potential risks we are facing. The General Counsel has significant prior business experience in compliance and risk management and coordinates directly with the third party who operates our SOC on issues involving particular cybersecurity expertise.

In an effort to help deter and detect cyber threats, we regularly provide all employees, including part-time and temporary employees, with data protection cybersecurity and incident prevention training throughout the year, which covers timely and relevant topics, including social engineering, phishing, password protection, confidential data protection, asset use and mobile security, and educates employees on the importance of reporting all incidents immediately. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

Item 2. Properties

Facilities

Our principal facilities consist of office and laboratory space in Philadelphia, Pennsylvania. We occupy approximately 4,369 square feet of office space under a lease that is expected to expire in October 2029 and approximately 3,600 square feet of laboratory space under a lease that expires in April 2024. We believe that our facilities are sufficient to meet our current needs.

Item 3. Legal Proceedings

We are currently not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

Part II

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

Holders of Our Common Stock

Our common stock is currently listed on the Nasdaq Stock Market under the symbol "CARM." The number of stockholders of record of our common stock as of March 15, 2024 was 42. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business. We do not anticipate paying any cash dividends for the foreseeable future, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. 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 issue any securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act, during the twelve months ended December 31, 2023, other than pursuant to transactions previously disclosed in our Current Reports on Form 8-K.

Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

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 together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth in the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated by these forward-looking statements.

Overview

We are a clinical-stage cell therapy company focused on using our proprietary CAR-M cell therapy platform to develop transformative immunotherapies to treat cancer and other serious diseases. We have created a comprehensive cell therapy platform to enable the therapeutic use of engineered macrophages and monocytes, which belong to a subgroup of white blood cells called myeloid cells. Our focus is our proprietary CAR-M cell therapy platform, which redirects macrophages against specific tumor associated antigens and enables targeted anti-tumor immunity by utilizing genetically modified myeloid cells (macrophages and monocytes) to express CARs, enabling these potent innate immune cells to recognize specific tumor associated antigens on the surface of tumor cells.

Our first product candidate to enter clinical development, CT-0508, is the first CAR-Macrophage to be evaluated in a human clinical trial and is intended to treat solid tumors that over-express HER2, a protein that is over-expressed on the surface of a variety of solid tumors, including breast cancer, gastric cancer, esophageal cancer, salivary gland cancer, and numerous others. CT-0508 is currently being studied in a multi-center open label Phase 1 clinical trial in the United States. This ongoing first-in-human study evaluates the safety, tolerability, and manufacturing feasibility of CT-0508 along with several customary exploratory secondary endpoints.

In late March 2024, following a strategic review of our operating plan for 2024 and future periods, we approved a revised operating plan intended to balance value creation and expense management with our available cash resources. The objective of our revised operating plan is to focus our clinical development efforts on high potential value programs with meaningful near-term milestones and eliminate non-essential expenses and headcount to extend our cash runway. Under this plan, we intend to focus our *ex vivo* oncology clinical development efforts on our follow-on product candidate CT-0525, a CAR-Monocyte intended to treat solid tumors that over-express HER2.

CT-0525 utilizes a novel approach to CAR-M therapy that engineers patients' monocytes directly, without *ex vivo* differentiation into macrophages. In November 2023, we received FDA clearance of our IND for CT-0525. We expect to treat the first patient in the second quarter of 2024 and to report preliminary data from the study by the end of 2024. We believe that CT-0525 has favorable attributes compared to our initial clinical stage product candidate, CT-0508, and that the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. We will also continue to focus on our *in vivo* mRNA/LNP CAR-M programs in partnership with Moderna.

Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities. We have also elected to pause further development of CT-1119, a mesothelin-targeted CAR-Monocyte, pending additional financing.

Our early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases, also remains ongoing.

We plan to pursue additional financing and collaboration opportunities to support development of our product candidates and other research and development programs and will continue to re-assess our expense allocation.

Our Pipeline

Using our proprietary macrophage and monocyte cell therapy platform, we are developing a pipeline of product candidates, with an initial focus on advancing *ex vivo* autologous and *in vivo* CAR-M therapies for the treatment of solid tumors. We are also pursuing early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Our *ex vivo* oncology, fibrosis, and immunology programs are wholly owned. Additionally, under the Moderna License Agreement with Moderna, we are

developing *in vivo* CAR-M therapies utilizing Moderna's mRNA/LNP technology. As part of the Moderna License Agreement, as further discussed below, we received a $45.0 million up-front cash payment and an investment by Moderna in the form of a $35.0 million convertible promissory note, which converted into shares of common stock in connection with the consummation of the Merger, in addition to future research funding and the opportunity for milestone payments and royalties.

Our follow-on product candidate, CT-0525, a CAR-Monocyte intended to treat solid tumors that over-express HER2, utilizes a novel approach to CAR-M therapy that engineers patients' monocytes directly, without *ex vivo* differentiation into macrophages, as we currently do for CT-0508. The CAR-Monocyte approach utilizes a single day manufacturing process, which enables the manufacture of up to ten billion cells from a single apheresis, and leverages an automated, closed-system manufacturing process. In addition, the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. By increasing the cell yield, a CAR-Monocyte enables a larger dose than a CAR-Macrophage. In addition, CAR-Monocyte has the potential for improved persistence and trafficking, which were observed in pre-clinical studies. We believe that the increased cell yield, and the improved persistence and trafficking may improve tumor control. In November 2023, we received FDA clearance of our IND for CT-0525 and we expect to treat the first patient in the second quarter of 2024.

In addition to the development of *ex vivo* CAR-M cell therapies, we are developing *in vivo* CAR-M cell therapies, wherein immune cells are directly engineered within the patient’s body. To advance our *in vivo* CAR-M therapeutics, we established the Moderna License Agreement. In the fourth quarter of 2023, we presented pre-clinical data from this collaboration demonstrating that CAR-M can be directly produced *in vivo*, successfully redirecting endogenous myeloid cells against tumor-associated antigens using mRNA/LNP. Additionally, the pre-clinical data demonstrated feasibility, tolerability, and early efficacy of *in vivo* CAR-M against metastatic solid tumors. In December 2023, we announced the nomination of the collaboration's first lead candidate, which will target an antigen present on a solid tumor with significant unmet medical need.

In addition to acting as a first line of defense in the innate immune system, macrophages and monocytes are found in all tissues in the body where they serve key regulatory functions such as wound healing, termination of immune responses and tissue regeneration. Using our macrophage and monocyte engineering platform, we are pursuing early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Pre-clinical proof of concept for fibrosis is expected in the second quarter of 2024.

To date, we have not yet commercialized any products or generated any revenue from product sales and have financed our operations primarily with proceeds from sales of our preferred stock, proceeds from our collaboration with Moderna, research tax credits, convertible debt financing, closing of pre-closing financing, and completion of the Merger. Our operations to date have been limited to organizing and staffing the company, business planning, capital raising, establishing and maintaining our intellectual property portfolio, building our pipeline of product candidates, conducting drug discovery activities, undertaking pre-clinical studies, manufacturing process development studies, conducting early-stage clinical trials, and providing general and administrative support for these operations. We have devoted substantially all of our financial resources and efforts to pursuing discovery, research and development of our product candidates.

Financial Operations

Our net losses were $86.9 million and $61.2 million for the year ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had $77.6 million in cash and cash equivalents and an accumulated deficit of $245.1 million. We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct our clinical trial of CT-0525 , complete our ongoing clinical trial of CT-0508 with respect to patients currently enrolled or in screening and advance our discovery programs and continue our product development efforts. If we obtain marketing approval for CT-0525 or any other product candidate we are developing or develop in the future, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. We believe our revised operating plan approved in March 2024 by our board of directors will facilitate cost control to support further development of our product candidates and other research and development programs.

As of December 31, 2023, we have 40,609,915 shares of common stock issued and outstanding. On March 7, 2023 in connection with the closing of the Merger, we issued 29,880,394 shares of common stock to Legacy Carisma stockholders (including 5,059,338 shares issued to the holder of the convertible promissory note that was entered into concurrently with the Moderna License Agreement (as defined below) and 3,730,608 shares issued in exchange for shares sold in the pre-

closing financing). Former Sesen Bio stockholders continued to hold 10,374,272 shares of our common stock, reflective of the 1-for-20 reverse stock split that was effected immediately prior to the closing of the Merger.We will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise additional capital or obtain adequate funds on acceptable terms, we may be required to further delay, limit, reduce or terminate our discovery and product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. However, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract from our discovery and product development efforts. Considering the anticipated benefits of our revised operating plan, we believe that we have cash and cash equivalents sufficient to sustain our operating expenses and capital expenditure requirements into the third quarter of 2025.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand business, maintain discovery and product development efforts, diversify our pipeline of product candidates or even continue operations.

Moderna Collaboration and License Agreement

In collaboration with Moderna, we have established an approach that uses Moderna's mRNA/LNP technology, together with our CAR-M platform technology, to create novel *in vivo* oncology gene therapies. We believe this approach has the potential to enable a series of off-the-shelf product candidates to target a patient's own myeloid cells against cancer cells directly within their body.

In January 2022, Legacy Carisma and Moderna established this collaboration by entering into the Moderna License Agreement, which provides for a broad strategic collaboration to discover, develop and commercialize *in vivo* engineered CAR-M therapeutics for up to 12 oncology programs. Under the Moderna License Agreement, the parties initiate research programs during a research term, focused on the discovery and research of products directed to biological targets. Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Moderna has the right to designate up to 12 research targets as development targets. The first five research targets have been nominated and all programs are currently in the discovery phase. Moderna funds the cost of our activities in accordance with an agreed research budget.

Moderna has the right to designate up to 12 research targets as development targets during a specified development target nomination period upon payment of a development target designation milestone payment. Moderna can replace development targets with research targets during a specified period of time. If Moderna exercises its right to designate a development target, Moderna will have a worldwide, exclusive license under patents and know-how controlled by us to develop and commercialize products directed to the applicable development target, subject to certain diligence obligations.

The collaboration is managed by a JSC, which is comprised of representatives from us and Moderna. Decisions of the JSC are made by consensus, with each party having one vote. If the JSC is unable to agree, and the parties' executives are not able to resolve the dispute, then Moderna has final decision-making authority, subject to specified limitations.

Commencing a specified time after the effective date of the Moderna License Agreement, Moderna will have the right to nominate targets relating to diseases outside the field of oncology for inclusion in research programs in specified circumstances. Such right is subject to the same exclusions as Moderna's right to nominate other targets for inclusion in research programs.

During the term of the Moderna License Agreement, we and our affiliates are subject to various exclusivity obligations under which we are not permitted to research, develop or commercialize particular products outside of the collaboration, including products for use as *in vivo* therapies in the field of oncology, products directed to any target included in the collaboration, or products containing a polypeptide provided by us to Moderna in connection with a research program that are directed to any development target.

Under the terms of the Moderna License Agreement, we received a $45.0 million up-front cash payment. Assuming Moderna develops and commercializes 12 products, each directed to a different development target, we are also eligible to receive up to between $247.0 million and $253.0 million per product in development target designation, development, regulatory and commercial milestone payments. Moderna also will reimburse us for all costs incurred in connection with our research and development activities under the Moderna License Agreement plus a reasonable margin for the respective services performed (with a minimum commitment to reimburse $10.0 million in research and development costs over the first three years from execution of the Moderna License Agreement). In addition, we are eligible to receive tiered mid-to-high single digit royalties on net product sales, which may be subject to reductions. Moderna has also agreed to cover the cost of certain milestone payments and royalties we owe to Penn as a licensor under one of our intellectual property in-license agreements that we are sublicensing to Moderna under the Moderna License Agreement, which royalties Moderna may deduct in part from any royalties owed to us. The Moderna License Agreement terminates on a product-by-product basis upon the latest of expiration of the applicable product patents, expiration of regulatory exclusivity and the tenth anniversary of first commercial sale, unless terminated earlier by us or Moderna.

Cost Reduction Measures

We have recently implemented a revised operating plan to reduce our monthly operating expenses and conserve cash. The plan, which we will begin to implement in the second quarter of 2024, includes several measures such as prioritizing CT-0525 as our anti-HER2 product candidate going forward, suspending the enrollment of new patients for CT-0508 in line with the clinical judgment of the clinical site principal investigator, pausing further development of CT-1119, reducing our workforce by 39 full-time employees (representing approximately 37% of our total workforce), including employees engaged in research and development and general and administration activities, and decreasing spending on other non-essential activities.

We believe these changes will provide operating efficiencies for us to continue to support our product development programs as well as any potential collaborations or other strategic relationships we may enter into. We expect to incur approximately $2.1 million in connection with the reduction in workforce, which primarily represents one-time employee termination benefits directly associated with the workforce reduction. We expect the reduction in workforce to be substantially complete and to pay the majority of these reduction in workforce amounts in the second quarter of 2024.

Financial Operations Overview

Collaboration Revenues

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 revenues to date have been generated from the Moderna License Agreement. Moderna reimburses us for all costs incurred by it in connection with its research and development activities under the Moderna License Agreement plus a reasonable margin for the respective services performed. We expect that our revenue for at least the next several years will be derived primarily from Moderna License Agreement, other current collaboration agreements and any additional collaborations that we may enter into in the future. To date, we have not received any royalties under the Moderna License Agreement.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including discovery efforts and the development of product candidates, and include:

- expenses incurred to conduct the necessary pre-clinical studies and clinical trials required to obtain regulatory approval;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- costs of funding research performed by third parties, including pursuant to agreements with CROs, as well as investigative sites and consultants that conduct our pre-clinical studies and clinical trials;
- expenses incurred under agreements with CMOs, including manufacturing scale-up expenses and the cost of acquiring and manufacturing pre-clinical study and clinical trial materials;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the costs of laboratory supplies and acquiring materials for pre-clinical studies;

- facility-related expenses, which include direct depreciation costs of equipment and expenses for rent and maintenance of facilities and other operating costs; and
- third-party licensing fees.

Research and development activities are central to our business model. Product candidates in later stages of clinical development will generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development expenses to decrease in 2024 as we implement our revised operating plan, including a reduction in workforce, prioritization of CT-0525 and a pause in development of CT-1119. We expect that our expenses will increase again in future years as we continue to advance our clinical trials and potentially progress additional product candidates.

The successful development of our current or future product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of any product candidates. The success of CT-0525 and our other product candidates will depend on several factors, including the following:

- successfully completing pre-clinical studies;
- successfully initiating future clinical trials;
- successfully enrolling patients in and completing clinical trials;
- scaling up manufacturing processes and capabilities to support clinical trials of CT-0525 and any other product candidate;
- applying for and receiving marketing approvals from applicable regulatory authorities;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for CT-0525 and any other product candidates the Company is developing or may develop in the future;
- making arrangements with third-party manufacturers, or establishing commercial manufacturing capabilities, for both clinical and commercial supplies of our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of CT-0525 and any other product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- maintaining, enforcing, defending and protecting our rights in our intellectual property portfolio;
- not infringing, misappropriating or otherwise violating others' intellectual property or proprietary rights; and
- maintaining a continued acceptable safety profile of our products following receipt of any marketing approvals.

A change in the outcome of any of these variables with respect to the development, manufacture or commercialization activities of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive, if there are safety concerns or if we determine that the observed safety or efficacy profile would not be competitive in the marketplace, we could be required to expend significant additional financial resources and time on the completion of clinical development. Product commercialization will take several years, and we expect to spend a significant amount in development costs.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel expenses, including salaries, benefits and stock-based compensation expense for employees in executive, finance, accounting, business development and human resource functions. General and administrative expense also includes corporate facility costs, including rent, utilities, depreciation and maintenance, and costs not otherwise included in research and development expenses, legal fees related to intellectual property and corporate matters as well as fees for accounting and consulting services.

We expect that our general and administrative expenses will decrease in 2024, as we implement our revised operating plan, including reducing our workforce and decreasing expenses related to non-essential activities. In addition, our 2023

expenses included a significant amount of non-recurring costs related to the Merger that are described below. We expect that our expenses will increase again in future years as we continue to incur costs associated with being a public company.

Interest Income (Expense)

Interest income consists of interest earned on our excess cash. Interest expense consisted of interest on our convertible promissory note that was entered into concurrently with the Moderna License Agreement including non-cash interest expense associated with the amortization of the debt discount. The convertible promissory note was converted into common stock upon the closing of the Merger.

Change in Fair Value of Derivative Liability

Change in fair value of the derivative liability for the redemption feature of our convertible promissory note reflected the non-cash charge for changes in the fair value of the derivative liability that was subject to re-measurement at each balance sheet date through the settlement of the convertible promissory note upon the closing of the Merger at which time the redemption feature was derecognized.

Income Taxes

Since inception, we have incurred significant net losses. As of December 31, 2023, we had NOLs for federal income tax purposes of $317.6 million. We have provided a valuation allowance against the full amount of our deferred tax assets since, in our opinion, based upon our historical and anticipated future losses, it is more likely than not that the benefits will not be realized. As of December 31, 2023, we remained in a full valuation allowance position.

The utilization of our NOLs may be subject to a substantial annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percent, as defined under Sections 382 and 383 of the Code, respectively, as well as similar state provisions. We have recorded a valuation allowance on all of our deferred tax assets, including deferred tax assets related to NOLs.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

	Year Ended December 31,	
	2023	2022
Collaboration revenues	$ 14,919	$ 9,834
Operating expenses:		
Research and development	74,125	56,618
General and administrative	29,525	9,378
Total operating expenses	103,650	65,996
Operating loss	(88,731)	(56,162)
Change in fair value of derivative liability	(84)	(1,919)
Interest income (expense), net	1,936	(3,145)
Net loss	$ (86,879)	$ (61,226)

Collaboration Revenues

Collaboration revenues were $14.9 million and $9.8 million for the years ended December 31, 2023 and 2022, respectively. The increase was related to the research and development activities completed under the Moderna License Agreement that we executed in January 2022.

Research and Development Expenses

We track outsourced development, outsourced personnel costs and other external research and development costs of our CT-0508, CT-0525, and CT-1119 programs. We do not track internal research and development costs on a program-by-

program basis. The following table summarizes our research and development expenses for the years ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,	
	2023	2022
CT-0508(1)	$ 12,354	$ 12,654
CT-0525	8,440	—
CT-1119(1)	928	—
Personnel costs, including stock-based compensation	20,637	16,233
Other clinical and pre-clinical development expenses	6,217	4,913
Facilities and other expenses	25,549	22,818
Total research and development expenses	$ 74,125	$ 56,618

(1) Although we plan to continue ongoing activities under our open label Phase 1 clinical trial of CT-0508 and our sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities. We have also elected to pause further development of CT-1119, a mesothelin-targeted CAR-Monocyte, pending additional financing.

Research and development expenses for the year ended December 31, 2023 were $74.1 million, compared to $56.6 million for the year ended December 31, 2022. The increase of $17.5 million was primarily due to a $8.4 million increase in direct costs associated with pre-clinical development of CT-0525, a $4.4 million increase in personnel costs due to growth in research and development employee headcount, a $2.7 million increase in our facilities and other expenses resulting from increased laboratory space and laboratory supplies from expanded clinical and pre-clinical work, a $1.3 million increase due to costs associated with growth and expansion of pre-clinical activities towards submission of an IND for CT-0525, and a $0.9 million increase in direct costs associated with the pre-clinical development related to CT-1119, partially offset by a $0.2 million decrease in direct costs associated with CT-0508.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,	
	2023	2022
Personnel costs, including stock-based compensation (1)	$ 12,555	$ 3,397
Professional fees	12,237	4,703
Facilities and supplies	1,390	601
Insurance, taxes, and fees	2,333	211
Other expenses	1,010	466
Total general and administrative expenses	$ 29,525	$ 9,378

(1) In March 2024, our board of directors approved the revised operating plan which includes the reduction in work force of certain finance and corporate employees.

General and administrative expenses for the year ended December 31, 2023 were $29.5 million, compared to $9.4 million for the year ended December 31, 2022. The increase of $20.1 million was primarily attributable to a $9.2 million increase of personnel costs and a $7.5 million increase in professional fees. The increase in personnel costs was primarily due to non-recurring severance and other costs associated with the Merger of $4.6 million and higher personnel costs as a result of an increase in headcount to support operating as a public company of $4.6 million. The increase in professional fees primarily consisted of $5.3 million in costs associated with activities to support the transitioning to and operating as a public company and protecting our IP portfolio, along with $2.2 million in legal fees and communication fees associated

with the Merger. Insurance and taxes increased $2.1 million as a result of costs associated with operating as a public company, such as director and officer insurance. Facilities and supplies increased $0.8 million due to office expenditures resulting from an increased footprint, and other expenses increased $0.5 million.

Interest Income (Expense), net

We recognized $1.9 million in interest income (expense), net for the year ended December 31, 2023, which was attributable primarily to interest income of $3.7 million, partially offset by $1.3 million the accelerated amortization of the debt discount as a result of the settlement of the convertible promissory note at the closing of the Merger, and $0.5 million interest expense on the outstanding principal balance associated with the convertible promissory note issued to Moderna through March 7, 2023.

We recognized $(3.1) million in interest income (expense), net for the year ended December 31, 2022, which was attributable primarily to interest expense on the outstanding principal balance associated with the convertible promissory note issued to Moderna, including non-cash interest expense associated with the amortization of the debt discount.

Change in Fair Value of Derivative Liability

We recognized a $0.1 million non-cash charge for the year ended December 31, 2023, for the increase in fair value of the derivative liability associated with the redemption feature of the convertible promissory note with Moderna through settlement in connection with the Merger.

We recognized a $1.9 million non-cash charge for the year ended December 31, 2022, for the increase in fair value of the derivative liability associated with the redemption feature of the convertible promissory note with Moderna, which was attributable to the timing in which we expected the accrued settlement event to occur.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2023, we had $77.6 million in cash and cash equivalents and an accumulated deficit of $245.1 million. To date, we have not yet commercialized any products or generated any revenue from product sales and have financed operations primarily with proceeds from sales of preferred stock, proceeds from our collaboration with Moderna, research tax credits and convertible debt financing. Under the Moderna License Agreement we anticipate receiving $73.9 million over the term of the contract for expected research and development services to be performed by Carisma, inclusive of pass-through costs, to be billed quarterly. Through December 31, 2023, we have generated $24.7 million of collaboration revenues related to research and development services. Under the terms of the Moderna License Agreement, assuming Moderna develops and commercializes 12 products, each directed to a different development target, we are eligible to receive up to between $247.0 million and $253.0 million per product in development target designation, development, regulatory and commercial milestone payments.

On April 17, 2023, we filed a universal shelf registration statement on Form S-3, which was declared effective on May 2, 2023, or the Registration Statement. Under the Registration Statement, we may offer and sell up to $300.0 million of a variety of securities, including debt securities, common stock, preferred stock, depository shares, subscription rights, warrants and units from time to time in one or more offerings at prices and on terms to be determined at the time of the offering. On May 12, 2023, we entered into an Amended and Restated Open Market Sale Agreement^{SM}, or the Sale Agreement, with Jefferies LLC, as sales agent, pursuant to which we may offer and sell shares of our common stock with an aggregate offering price of up to $100.0 million under an “at-the-market" offering program. As of December 31, 2023,

we have sold 226,533 shares for gross proceeds of $0.6 million. From January through March 2024, the Company sold an additional 931,250 shares for gross proceeds of $2.4 million.

Cash Flows

The following table shows a summary of our cash flows for the year ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,	
	2023	2022
Cash (used in) provided by		
Operating activities	$ (81,177)	$ (5,116)
Investing activities	72,408	(32,560)
Financing activities	62,180	33,319
Net change in cash and cash equivalents	$ 53,411	$ (4,357)

Cash Flows from Operating Activities

During the year ended December 31, 2023, we used $81.2 million of net cash in operating activities. Cash used in operating activities reflected our net loss of $86.9 million and a $5.4 million net change in our operating assets and liabilities attributable to the timing in which we pay our vendors for research and development activities that was offset by $11.1 million of non-cash charges related to depreciation and amortization expense, stock-based compensation, reductions in the operating right of use, or ROU assets, amortization of the debt discount on the convertible promissory note, change in fair value of the derivative liability, accretion on marketable securities, and non-cash interest on the finance lease liability.

During the year ended December 31, 2022, we used $5.1 million of net cash in operating activities. Cash provided by our operating activities reflected our net loss of $61.2 million that was offset by $10.9 million of non-cash charges related to depreciation and amortization expense, stock-based compensation, reductions in the operating ROU assets, amortization of the debt discount on the convertible promissory note, change in fair value of the derivative liability, non-cash interest on the finance liability from the failed sale-leaseback and the accretion on marketable securities, and a $45.2 million net change in our operating assets and liabilities which was primarily attributable to the $45.0 million upfront nonrefundable payment received from Moderna pursuant to the Moderna License Agreement.

Cash Flows from Investing Activities

During the year ended December 31, 2023, we received $72.4 million of net cash from investing activities. Cash provided by investing activities reflected $108.0 million of proceeds from the sale of marketable securities, partially offset by purchases of marketable securities of $34.5 million and the purchase of property and equipment of $1.1 million.

During the year ended December 31, 2022, we used $32.6 million of net cash in investing activities. Cash used in investing activities reflected purchases of marketable securities of $90.9 million and $4.7 million of purchases of property and equipment, partially offset by $63.0 million of proceeds from the sale of marketable securities.

Cash Flows from Financing Activities

During the year ended December 31, 2023, we received $62.2 million of net cash from financing activities, primarily attributable to the $37.9 million in the cash and cash equivalents acquired in connection with the Merger, $30.6 million in proceeds from the issuance of common stock in pre-closing financing, $1.2 million in proceeds from failed-sale leaseback arrangements, $0.6 million from the sale of common stock in connection with the Sale Agreement, partially offset by $5.8 million in payments of financing costs, $1.3 million in payments of principal related to finance lease liabilities, and $1.1 million in payments to our finance liability from failed sale-leaseback arrangements.

During the year ended December 31, 2022, we received $33.3 million of net cash from financing activities primarily attributable to the $35.0 million in proceeds from convertible promissory note and $1.6 million in proceeds from the failed sale-leaseback arrangements, partially offset by $2.5 million in payments made on deferred financing costs and $0.9 million in payments made on financing leases.

Funding Requirements

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct our planned clinical trial of CT-0525, advance our discovery programs and continue our product development efforts. As of December 31, 2023, we had cash and cash equivalents of $77.6 million. We believe that the revised operating plan approved in March 2024 by our board of directors will reduce our spending such that our liquidity is sufficient to sustain our operating expenses and capital expenditure requirements into the third quarter of 2025. We have based our estimate regarding the sufficiency of our cash resources on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us.

We expect our expenses to increase substantially over time in connection with our ongoing activities, particularly as we advance our pre-clinical activities and clinical trials. In addition, if we obtain marketing approval for CT-0525 or any other product candidate we are developing or develop in the future, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. In addition, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise additional capital or obtain adequate funds when needed or on acceptable terms, we may be required to further delay, limit, reduce or terminate our discovery and product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market on our own. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and distract us from discovery and product development efforts.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing clinical trial of CT-0525 and other planned and future clinical trials;
- the costs of our clinical trials of CT-0508 with respect to patients currently enrolled or in screening;
- the scope, progress, costs and results of pre-clinical testing and clinical trials of CT-0525 for additional combinations, targets and indications;
- the number of and development requirements for additional indications for CT-0525 or for any other product candidates;
- the success of our collaborations with Moderna or others;
- our ability to scale up our manufacturing processes and capabilities to support clinical trials of CT-0525 and other product candidates we are developing and develop in the future;
- the costs, timing and outcome of regulatory review of CT-0525 and other product candidates we are developing and may develop in the future;
- potential changes in the regulatory environment and enforcement rules;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment of license fees and other costs of our technology license arrangements;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for CT-0525 and other product candidates we are developing and may develop in the future for which we may receive marketing approval;
- our ability to obtain and maintain acceptance of any approved products by patients, the medical community and third-party payors;
- the amount and timing of revenue, if any, received from commercial sales of CT-0525 and any other product candidates we are developing or develop in the future for which we receive marketing approval;
- potential changes in pharmaceutical pricing and reimbursement infrastructure;
- the availability of raw materials for use in production of our product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we in-license or acquire additional technologies or product candidates.

Identifying potential product candidates and conducting pre-clinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. We will not generate commercial revenues unless and until we can achieve sales of products, which we do not anticipate for a number of years, if at all. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms,

or at all, and may be impacted by the economic climate and market conditions. For example, market volatility resulting from general U.S. or global economic or market conditions, including related to any health epidemics, pandemics or other contagious outbreaks (including any resurgence of the COVID-19 pandemic), could also adversely impact our ability to access capital as and when needed.

Alternatively, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Until such time, if ever, we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. 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 those securities may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. Debt financing and preferred equity financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our operations and ability to take specific actions, such as incurring additional debt, making acquisitions, engaging in acquisition, merger or collaboration transactions, selling or licensing our assets, making capital expenditures, redeeming our stock, making certain investments, declaring dividends or other operating restrictions that could adversely impact our ability to conduct business.

If we raise funds through additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, discovery programs or product candidates, grant licenses on terms that may not be favorable to us or grant rights to develop and market product candidates that we would otherwise prefer to develop and market on our own, any of which may have a material adverse effect on our business, operating results and prospects. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to further delay, limit, reduce or terminate our discovery and product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market on our own.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments at December 31, 2023 (in thousands):

	Total	Less than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 Years
Contractual obligations:					
Operating lease commitments[1]	$ 2,612	$ 1,510	$ 678	$ 424	$ —
Finance lease commitments	939	600	339	—	—
Manufacturing commitments[2]	4,000	1,000	3,000	—	—
Total contractual obligations	$ 7,551	$ 3,110	$ 4,017	$ 424	$ —

(1) Reflects obligations pursuant to our office and laboratory leases in Philadelphia, Pennsylvania.
(2) Reflects obligations pursuant to a manufacturing and supply agreement pursuant to which we will pay $1.0 million per calendar year, payable in quarterly payments, for reserved capacity starting on the date on which the manufacturing site is declared ready to produce CT-0508 as determined by us. In the event of termination without cause by us, our future commitments will cease and a termination fee equal to $4.0 million will be payable by us to Novartis which, pursuant to the terms of the agreement, can be credited in full against amounts due for a substitute product.

The commitment amounts in the table above are associated with contracts that are enforceable and legally binding and that specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts. Our contracts with CMOs, CROs and other third parties for the manufacture of our product candidates and to support pre-clinical research studies and clinical testing are generally cancelable by us upon prior notice and do not contain any minimum purchase commitments. Payments due upon cancellation consisting only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation are not included in the table above as the amount and timing of such payments are not known.

The table above does not include any potential milestone or royalty payments that we may be required to make under our license agreement with Penn (as defined below) and under licensing agreements with other third parties not considered material. We excluded these milestone and royalty payments given that the timing and likelihood of any such payments cannot be reasonably estimated at this time.

Penn License

In November 2017, we entered into a license agreement with Penn for certain intellectual property licenses, which was amended in February 2018, January 2019, March 2020 and June 2021. We are responsible for paying Penn an annual license maintenance fee in the low tens of thousands of dollars, payable until our first payment of a royalty. We may be required to pay Penn up to $10.9 million per product in development and regulatory milestone payments, up to $30.0 million per product in commercial milestone payments, and up to an additional $1.7 million in development and regulatory milestone payments for the first CAR-M product directed to mesothelin. While the agreement remains in effect, we are required to pay Penn low- to mid-single digit percentage tiered royalties on annual net sales of licensed products, which may be subject to reductions. Penn is guaranteed a minimum royalty payment amount in the low hundreds of thousands of dollars for each year after the first commercial sale of a licensed product. We must also pay Penn a percentage in the mid-single digits to low double digits of certain types of income we receive from sublicensees. In addition, we are required to pay Penn an annual alliance management fee in the low tens of thousands of dollars, ending after several years, unless we provide funding to Penn for research and development activities that extend beyond a specified date, in which case we will continue to owe the alliance management fee for each year in which we continue to fund such activities. We also paid Penn an upfront fee in the low hundreds of thousands of dollars for the license to the patents related to the mesothelin binder that is incorporated into the CAR design for our mesothelin product candidate. We are responsible for a pro rata share of costs relating to the prosecution and maintenance of the licensed patents.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on our limited historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 3 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies are the most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenues from Contracts

We account for our revenue in accordance with Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, or ASC 606. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps at inception of the agreement or upon material modification of the agreement: (i) identifies the contract(s) with a customer; (ii) identifies the performance obligations in the contract; (iii) determines the transaction price, including variable consideration, if any; (iv) allocates the transaction price to the performance obligations in the contract; and (v) recognizes revenue when (or as) the entity satisfies a performance obligation.

We consider the pattern of satisfaction of the performance obligations under step (v) above to be a critical accounting estimate. More specifically, the determination of the level of achievement of research and development service performance obligations, whose pattern of satisfaction is measured using costs incurred to date as compared to total costs incurred and expected to be incurred in the future is driven by a critical accounting estimate.

In estimating the costs expected to be incurred in the future, we use our most recent budget and long-range plan, adjusted for any pertinent information. While this is our best estimate as of the reporting period, costs expected to be incurred in the

future require managements judgment as the scope and timing of research and development activities may change significantly over time. We may adjust the scope of our research and development activities based on several factors, such as additional work needed to support advancement of product candidate or change in the number of patients in trials. Further, research and development services may no longer be within the scope of a collaboration agreement, as has been the case with certain of our programs. The timing of when research and development costs are expected to be incurred may change as a result of external factors, such as delays caused by manufacturing or supply chain, or difficulty in enrolling patients; or internal factors, such as prioritization of programs. Our estimate of the scope and timing of research and development services performed relative to the actual scope and timing may have a significant impact on revenue recognition.

Research and Development Accruals

Research and development expenses consist primarily of costs incurred in connection with the development of our product candidates. We expense research and development costs as incurred.

We accrue expenses for pre-clinical studies and activities performed by third parties based upon estimates of the proportion of work completed over the term of the individual trial and patient enrollment rates in accordance with agreements with third parties. We determine the estimates by reviewing contracts, vendor agreements and purchase orders, and through discussions with our internal clinical personnel and external service providers as to the progress or stage of completion of activities or services and the agreed-upon fee to be paid for such services. However, actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known at that time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly. Non-refundable advance payments for goods and services, including fees for process development or manufacturing and distribution of pre-clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Milestone payments within our licensing and collaboration arrangements are recognized when achievement of the milestone is deemed probable to occur. To the extent products are commercialized and future economic benefit has been established, commercial milestones that become probable are capitalized and amortized over the estimated remaining useful life of the intellectual property. In addition, we accrue royalty expense and sublicense non-royalty payments, as applicable, for the amount we are obligated to pay, with adjustments as sales are made.

Stock-Based Compensation

We measure compensation expense for all stock-based awards based on the estimated fair value of the award on the grant date. We use the Black-Scholes option pricing model to value our stock option awards. We recognize compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the award. We have not issued awards where vesting is subject to a market or performance condition.

The Black-Scholes option pricing model requires the use of subjective assumptions that include the expected stock price volatility and prior to the merger, the fair value of the underlying common stock on the date of grant. See Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted during the years ended December 31, 2023 and 2022.

Recent Accounting Pronouncements

See Note 3 to our consolidated financial statements found in this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our financial statements.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, including entities sometimes referred to as structured finance or special purpose entities that were established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. We do not engage in off-balance sheet financing arrangements. In addition, we do not engage in trading activities involving non-exchange traded contracts. We therefore believe that we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash, cash equivalents and marketable securities. Interest income earned on these assets was $3.7 million and $0.5 million for the year ended December 31, 2023 and 2022, respectively. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we may contract with foreign vendors. As such, our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2023 and 2022.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Carisma Therapeutics Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Carisma Therapeutics Inc. and subsidiaries (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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 audit to obtain reasonable assurance about whether the consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2018

Philadelphia, Pennsylvania
April 1, 2024

CARISMA THERAPEUTICS INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 77,605	$ 24,194
Marketable securities	—	27,802
Prepaid expenses and other assets	2,866	2,596
Total current assets	80,471	54,592
Property and equipment, net	6,764	8,628
Right of use assets – operating leases	2,173	4,822
Deferred financing costs	146	4,111
Total assets	$ 89,554	$ 72,153
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 3,933	$ 1,728
Accrued expenses	7,662	10,361
Deferred revenue	1,413	2,459
Operating lease liabilities	1,391	3,437
Finance lease liabilities	544	1,162
Other current liabilities	965	523
Total current liabilities	15,908	19,670
Deferred revenue	45,000	45,000
Convertible promissory note	—	33,717
Derivative liability	—	5,739
Operating lease liabilities	860	976
Finance lease liabilities	328	872
Other long-term liabilities	926	1,041
Total liabilities	63,022	107,015
Commitments and contingencies (Note 7)		
Convertible preferred stock	—	107,808
Stockholders' equity (deficit):		
Preferred stock $0.001 par value, 5,000,000 shares authorized, none issued or outstanding	—	—
Common stock $0.001 par value, 350,000,000 shares authorized, 40,609,915 and 2,217,737 shares issued and outstanding at December 31, 2023 and 2022, respectively	40	2
Additional paid-in capital	271,594	1,197
Accumulated other comprehensive loss	—	(41)
Accumulated deficit	(245,102)	(158,223)
Total Carisma Therapeutics Inc. stockholders' equity (deficit)	26,532	(157,065)
Noncontrolling interests	—	14,395
Total stockholders' equity (deficit)	26,532	(142,670)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 89,554	$ 72,153

See accompanying notes to consolidated financial statements.

CARISMA THERAPEUTICS INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2023	2022
Collaboration revenues	$ 14,919	$ 9,834
Operating expenses:		
Research and development	74,125	56,618
General and administrative	29,525	9,378
Total operating expenses	103,650	65,996
Operating loss	(88,731)	(56,162)
Change in fair value of derivative liability	(84)	(1,919)
Interest income (expense), net	1,936	(3,145)
Net loss	$ (86,879)	$ (61,226)
Share information:		
Net loss per share of common stock, basic and diluted	$ (2.59)	$ (28.77)
Weighted-average shares of common stock outstanding, basic and diluted	33,524,197	2,128,069
Comprehensive loss		
Net loss	$ (86,879)	$ (61,226)
Unrealized gain (loss) on marketable securities	440	(41)
Less: reclassification to net loss of previous unrealized gain on marketable securities	(399)	—
Comprehensive loss	$ (86,838)	$ (61,267)

See accompanying notes to consolidated financial statements.

CARISMA THERAPEUTICS INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Convertible preferred stock		Stockholders' Equity (Deficit)						
			Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Noncontrolling interests	Total
	Shares	Amount	Shares	Amount					
Balance, December 31, 2021	8,700,885	$ 107,808	2,059,072	$ 2	$ 816	$ —	$ (96,997)	$ 14,395	$ (81,784)
Exercise of stock options	—	—	158,665	—	106	—	—	—	106
Stock-based compensation	—	—	—	—	275	—	—	—	275
Unrealized loss on marketable securities	—	—	—	—	—	(41)	—	—	(41)
Net loss	—	—	—	—	—	—	(61,226)	—	(61,226)
Balance, December 31, 2022	8,700,885	107,808	2,217,737	2	1,197	(41)	(158,223)	14,395	(142,670)
Exercise of stock options	—	—	128,716	—	187	—	—	—	187
Stock-based compensation	—	—	—	—	2,316	—	—	—	2,316
Unrealized gain on marketable securities	—	—	—	—	—	440	—	—	440
Reclassification to net loss of previous unrealized gain on marketable securities	—	—	—	—	—	(399)	—	—	(399)
Issuance of common stock for cash in pre-closing financing	—	—	3,730,608	4	30,636	—	—	—	30,640
Issuance of common stock upon settlement of convertible promissory note, accrued interest, and related derivative liability	—	—	5,059,338	5	42,442	—	—	—	42,447
Issuance of common stock to Sesen Bio shareholders in reverse capitalization	—	—	10,374,272	10	72,034	—	—	—	72,044
Conversion of convertible preferred stock and non-controlling interests to common stock	(8,700,885)	(107,808)	18,872,711	19	122,185	—	—	(14,395)	107,809
Sale of common stock under Open Market Sales Agreement, net of issuance costs	—	—	226,533	—	597	—	—	—	597
Net loss	—	—	—	—	—	—	(86,879)	—	(86,879)
Balance, December 31, 2023	—	$ —	40,609,915	$ 40	$ 271,594	$ —	$ (245,102)	$ —	$ 26,532

See accompanying notes to consolidated financial statements.

CARISMA THERAPEUTICS INC.
Consolidated Statement of Cash Flows (in thousands)

	Year Ended December 31,	
	2023	**2022**
Cash flows from operating activities:		
Net loss	$ (86,879)	$ (61,226)
Adjustment to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation and amortization expense	2,837	1,893
Loss on disposal of property and equipment	159	—
Stock-based compensation expense	2,316	275
Reduction in the operating right of use assets	5,428	4,197
Amortization of debt discount	1,283	2,537
Change in fair value of derivative liability	84	1,919
Accretion on marketable securities	(709)	—
Realized gain on marketable securities	(399)	—
Non-cash interest expense	139	93
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	1,046	(1,361)
Accounts payable	2,191	(473)
Accrued expenses	(2,899)	4,230
Deferred revenue	(1,046)	47,459
Operating lease liabilities	(4,941)	(4,659)
Other long term liabilities	213	—
Net cash used in operating activities	(81,177)	(5,116)
Cash flows from investing activities:		
Purchase of marketable securities	(34,460)	(90,900)
Proceeds from the sale of marketable securities	108,000	63,000
Purchases of property and equipment	(1,132)	(4,660)
Net cash provided by (used in) investing activities	72,408	(32,560)
Cash flows from financing activities:		
Cash, cash equivalents and restricted cash acquired in connection with the reverse recapitalization	37,903	—
Payment of reverse recapitalization finance costs	(5,814)	—
Proceeds from the issuance of common stock in pre-closing financing	30,640	—
Payment of principal related to finance lease liabilities	(1,301)	(865)
Proceeds from failed sale-leaseback arrangement	1,183	1,626
Payment of finance liability from failed sale-leaseback arrangements	(1,069)	(98)
Payment of deferred financing costs	(146)	(2,450)
Proceeds from issuance of convertible promissory note	—	35,000
Proceeds from the exercise of stock options	187	106
Sale of common stock under Open Market Sales Agreement, net of issuance costs	597	—
Net cash provided by financing activities	62,180	33,319
Net increase (decrease) in cash and cash equivalents	53,411	(4,357)
Cash and cash equivalents at beginning of the year	24,194	28,551
Cash and cash equivalents at end of the year	$ 77,605	$ 24,194

See accompanying notes to consolidated financial statements.

CARISMA THERAPEUTICS INC.
Consolidated Statement of Cash Flows (in thousands)

Supplemental disclosures of cash flow information:		
Cash paid for interest	$ 352	$ 98
Supplemental disclosure of non-cash financing and investing activities:		
Conversion of convertible preferred stock and non-controlling interests upon Merger	$ 122,204	$ —
Conversion of convertible promissory note, accrued interest and derivative liability upon Merger	$ 42,447	$ —
Unrealized gain (loss) on marketable securities	$ 41	$ (41)
Deferred financing costs in accrued expenses	$ —	$ 1,661
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 2,779	$ 6,440
Right-of-use assets obtained in exchange for new financing lease liabilities	$ —	$ 2,898
Allocation of debt proceeds to derivative liability	$ —	$ 3,820

See accompanying notes to consolidated financial statements.

(1) Background

Overview

Carisma Therapeutics Inc., a Delaware corporation (collectively with its subsidiaries, the Company), is a clinical-stage cell therapy company focused on using the Company's proprietary chimeric antigen receptor macrophage and monocyte (CAR-M) cell therapy platform to develop transformative immunotherapies to treat cancer and other serious diseases. The Company has created a comprehensive cell therapy platform to enable the therapeutic use of engineered macrophages and monocytes, which belong to a subgroup of white blood cells called myeloid cells. The Company's focus is its proprietary CAR-M cell therapy platform, which redirects macrophages against specific tumor associated antigens and enables targeted anti-tumor immunity by utilizing genetically modified myeloid cells (macrophages and monocytes) to express chimeric antigen receptors (CARs), enabling these potent innate immune cells to recognize specific tumor associated antigens on the surface of tumor cells.

In March 2024, the Company and its board of directors approved a revised operating plan to reduce monthly operating expenses and conserve cash. The plan, which will be implemented in the second quarter of 2024, includes several measures such as prioritizing CT-0525 as the Company's anti-human epidermal growth factor receptor 2 (HER2) product candidate going forward, suspending the enrollment of new patients for CT-0508 in line with the clinical judgment of the clinical site principal investigator, pausing further development of CT-1119, reducing the workforce, including employees engaged in research and development and general and administration activities, and decreasing spending on other non-essential activities. The Company expects the reduction in workforce to be substantially complete and to pay the majority of the workforce reduction costs in the second quarter of 2024. The revised operating plan considers expenses pertaining to severance costs and potential termination and exit fees.

The Company's first product candidate to enter clinical development, CT-0508, is the first CAR-Macrophage to be evaluated in a human clinical trial and is intended to treat solid tumors that over-express HER2, a protein that is over-expressed on the surface of a variety of solid tumors, including breast cancer, gastric cancer, esophageal cancer, salivary gland cancer, and numerous others. CT-0508 has been granted "Fast Track" status for the treatment of patients with HER2 over-expressing solid tumors by the United States FDA. CT-0508 is currently being studied in a multi-center open label Phase 1 clinical trial in the United States. This ongoing first-in-human study evaluates the safety, tolerability, and manufacturing feasibility of CT-0508 along with several customary exploratory secondary endpoints.

CT-0525 utilizes a novel approach to CAR-M therapy that engineers patients' monocytes directly, without *ex vivo* differentiation into macrophages. In November 2023, the Company received FDA clearance of the Company's IND for CT-0525, and expects to treat the first patient in the second quarter of 2024. The Company believes that CT-0525 has favorable attributes compared to its initial clinical stage product candidate, CT-0508, and that the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. The Company will also continue to focus on its *in vivo* mRNA/lipid nanoparticle (LNP) CAR-M programs in partnership with Moderna.

Although the Company plans to continue ongoing activities under its open label Phase 1 clinical trial of CT-0508 and its sub-study utilizing CT-0508 in combination with pembrolizumab, enrollment of new patients will be suspended in line with the clinical judgment of the clinical site principal investigator. All patients currently enrolled or in screening will continue participation per protocol through the end of study milestone and will complete all required activities. The Company has also elected to pause further development of CT-1119, a mesothelin-targeted CAR-Monocyte, pending additional financing.

The Company's early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases, also remains ongoing.

Pipeline

Using its proprietary macrophage and monocyte cell therapy platform, the Company is developing a pipeline of product candidates with an initial focus on advancing multiple *ex vivo* autologous and *in vivo* CAR-M therapies for the treatment of solid tumors. The Company is also pursuing early research and development of multiple assets for the potential treatment

of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. The Company's *ex vivo* oncology, fibrosis, and immunology programs are wholly owned. Additionally, under a collaboration agreement (the Moderna License Agreement), with ModernaTX Inc. (Moderna) (Note 12), the Company is developing *in vivo* CAR-M therapies utilizing Moderna's mRNA/LNP technology.

The Company's follow-on product candidate, CT-0525, a CAR-Monocyte intended to treat solid tumors that over-express HER2, utilizes a novel approach to CAR-M therapy that engineers patients' monocytes directly, without *ex vivo* differentiation into macrophages, as the Company currently does for CT-0508. The CAR-Monocyte approach utilizes a single day manufacturing process, which enables the manufacture of up to ten billion cells from a single apheresis, and leverages an automated, closed-system manufacturing process. In addition, the CAR-Monocyte approach has the potential to improve upon the potential anti-tumor effect of a CAR-Macrophage. By increasing the cell yield, a CAR-Monocyte enables a larger dose than a CAR-Macrophage. In addition, CAR-Monocyte has the potential for improved persistence and trafficking, which were observed in pre-clinical studies. The Company believes that the increased cell yield, and the improved persistence and trafficking may improve tumor control. In November 2023, the Company received FDA clearance of its IND for CT-0525 and the Company expects to treat the first patient in the second quarter of 2024.

In addition to the development of *ex vivo* CAR-M cell therapies, the Company is developing *in vivo* CAR-M cell therapies, wherein immune cells are directly engineered within the patient's body. To advance the Company's *in vivo* CAR-M therapeutics, the Company established a strategic collaboration with Moderna (Note 12). In the fourth quarter of 2023, the Company presented pre-clinical data from this collaboration demonstrating that CAR-M can be directly produced *in vivo*, successfully redirecting endogenous myeloid cells against tumor-associated antigens using mRNA/LNP. Additionally, the pre-clinical data demonstrated feasibility, tolerability, and early efficacy of *in vivo* CAR-M against metastatic solid tumors. In December 2023, the Company announced the nomination of the collaboration's first lead candidate, which will target an antigen present on a solid tumor with significant unmet medical need.

In addition to acting as a first line of defense in the innate immune system, macrophages and monocytes are found in all tissues in the body where they serve key regulatory functions such as wound healing, termination of immune responses and tissue regeneration. Using the Company's macrophage and monocyte engineering platform, the Company is pursuing early research and development of multiple assets for the potential treatment of diseases beyond oncology, including fibrosis and other immunologic and inflammatory diseases. Pre-clinical proof of concept for fibrosis is expected in the first half of 2024.

Reverse Merger with Sesen Bio

On March 7, 2023, the Company (formerly publicly-held Sesen Bio, Inc.) consummated a merger with CTx Operations, Inc. (formerly privately-held CARISMA Therapeutics Inc.) (Legacy Carisma) pursuant to an Agreement and Plan of Merger and Reorganization, as amended (the Merger Agreement), by and among the Company, Legacy Carisma and Seahawk Merger Sub, Inc. (Merger Sub), a Delaware corporation and wholly-owned subsidiary of the Company. The Merger Agreement provided for the merger of Merger Sub with and into Legacy Carisma, with Legacy Carisma continuing as a wholly-owned subsidiary of the Company and the surviving corporation of the merger (the Merger). Pursuant to the Merger Agreement, the Company changed its name from "Sesen Bio, Inc." to "Carisma Therapeutics Inc." At the closing of the Merger, (a) each then outstanding share of Legacy Carisma common stock and convertible preferred stock (including shares of Legacy Carisma common stock issued in connection with the pre-closing financing transaction described below) were converted into shares of Sesen Bio, Inc. (Sesen Bio) common stock at an exchange ratio of 1.8994 shares of Sesen Bio for each share of Legacy Carisma (the Exchange Ratio), and (b) each then outstanding stock option to purchase Legacy Carisma common stock was assumed by Sesen Bio, with necessary adjustments to reflect the Exchange Ratio.

Except as otherwise indicated, references herein to "Carisma," the "Company," or the "Combined Company," refer to Carisma Therapeutics Inc. on a post-Merger basis, and references to "Legacy Carisma" refer to the business of privately-held CARISMA Therapeutics Inc. prior to the completion of the Merger. References to "Sesen Bio" refer to Sesen Bio, Inc. prior to the completion of the Merger.

Following the Merger, the shareholders of Legacy Carisma held 74.2% of the Combined Company and the shareholders of Sesen Bio held 25.8% of the Combined Company.

Exchange Ratio

As discussed in Note 4, the Merger was accounted for as reverse capitalization under which the historical financial statements of the Company prior to the Merger are Legacy Carisma. All common stock, per share and related information presented in the consolidated financial statements and notes prior to the Merger has been retroactively adjusted to reflect the Exchange Ratio.

(2) Development-Stage Risks and Liquidity

The accompanying consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The Company has incurred losses and negative cash flows from operations since inception and has an accumulated deficit of $245.1 million as of December 31, 2023. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales from its product candidates currently in development. As of December 31, 2023, the Company had $77.6 million of cash and cash equivalents. Absent any other action, the Company would have required additional liquidity to continue its operations over the next 12 months, which would have raised substantial doubt about its ability to continue as a going concern. As discussed in Note 1, Background, in March 2024, the Company and its board of directors approved a revised operating plan that suspends certain development programs, reduces its workforce and decreases other non-essential activities to extend the Company's cash runway. The Company projects this revised operating plan will alleviate the substantial doubt that has been raised by significantly decreasing expenses, thereby reducing ongoing liquidity needs to enable the continuation of operations for at least 12 months from the issuance date of these consolidated financial statements.

The Company is subject to those risks associated with any specialty biotechnology company that has substantial expenditures for research and development. There can be no assurance that the Company's research and development projects will be successful, that products developed will obtain necessary regulatory approval, or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants.

(3) Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). Any references in these notes to applicable guidance is meant to refer to GAAP as found in Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) promulgated by the Financial Accounting Standards Board (FASB).

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from such estimates. Estimates and assumptions are periodically reviewed, and the effects of revisions are reflected in the consolidated financial statements in the period they are determined to be necessary.

Significant areas that require management's estimates include the fair value of the Company's common stock and the derivative liability prior to the Merger, stock-based compensation assumptions, the estimated useful lives of property and equipment, and accrued research and development expenses.

Fair Value of Financial Instruments

Management believes that the carrying amounts of the Company's financial instruments, including cash equivalents and accounts payable, approximate fair value due to the short-term nature of those instruments. The Company considered the carrying value of its convertible promissory note (Note 8) as of December 31, 2022 to approximate fair value due to its short-term nature. The derivative liability was recorded at its estimated fair value prior to its derecognition in March 2023 upon conversion of the associated convertible promissory notes.

Fair Value Measurements

The Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible. The Company determines fair value based on assumptions that market participants would use in pricing an asset or liability in the principal or most advantageous market. When considering market participant assumptions in fair value measurements, the following fair value hierarchy distinguishes between observable and unobservable inputs, which are categorized in one of the following levels:

- Level 1 Inputs: Unadjusted quoted prices in active markets for identical assets or liabilities accessible to the reporting entity at the measurement date.

- Level 2 Inputs: Other than quoted prices included in Level 1 inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the asset or liability.

- Level 3 Inputs: Unobservable inputs for the asset or liability used to measure fair value to the extent that observable inputs are not available, thereby allowing for situations in which there is little, if any, market activity for the asset or liability at the measurement date.

The following fair value hierarchy table presents information about the Company's assets and liabilities measured at fair value on a recurring basis:

	Fair value measurement at reporting date using		
(in thousands)	(Level 1)	(Level 2)	(Level 3)
December 31, 2023			
Assets:			
Cash equivalents – money markets accounts	$ 62,999	$ —	$ —
December 31, 2022			
Assets:			
Cash equivalents – money markets accounts	$ 7,794	$ —	$ —
Marketable securities – U.S. Treasuries	$ 27,802	$ —	$ —
Liability:			
Derivative liability – redemption feature on convertible promissory note	$ —	$ —	$ 5,739

As of December 31, 2023, the Company had no marketable securities. The following is a summary of the Company's available-for-sale marketable securities as of December 31, 2022:

	Amortized cost	Gross unrealized loss	Fair value
U.S. Treasury securities	$ 27,843	$ (41)	$ 27,802

The Company evaluated a redemption feature within the convertible promissory note issued in January 2022 and determined bifurcation of the redemption feature was required. The redemption feature is classified as a liability on the accompanying consolidated balance sheet and is marked-to-market each reporting period with the changes in fair value

recorded in the accompanying statements of operations until it is triggered, terminated, reclassified or otherwise settled. The fair value of the derivative was determined based on an income approach that identified the cash flows using a with-and-without valuation methodology. The inputs used to determine the estimated fair value of the derivative instrument were based primarily on the probability of an underlying event triggering the embedded derivative occurring and the timing of such event.

During the year ended December 31, 2022, the discount factor used was 12% and a 90% to 100% probability of completing a qualified financing prior to the maturity date of the convertible promissory note was assumed. The estimated time of conversion ranged from three to twelve months.

The table presented below is a summary of the changes in fair value of the Company's derivative liability associated with the redemption feature of the Company's convertible promissory note (Level 3 measurement):

	Year Ended December 31,	
(in thousands)	2023	2022
Balance at the beginning of the period	$ 5,739	$ —
Balance at issuance	—	3,820
Change in fair value	84	1,919
Derecognition upon conversion of convertible promissory note	(5,823)	—
Balance at the end of the period	$ —	$ 5,739

During the year ended December 31, 2023 and 2022, there were no transfers between Level 1, Level 2 and Level 3.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* (ASC 606). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

The Company enters into collaboration and licensing agreements with strategic partners, which are within the scope of ASC 606, under which it may exclusively license rights to research, develop, manufacture, and commercialize its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: (1) non-refundable, upfront license fees (2) reimbursement of certain costs; (3) customer option fees for additional goods or services; (4) development milestone payments, (5) regulatory and commercial milestone payments; and (6) royalties on net sales of licensed products.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use its judgment to determine: (a) the number of performance obligations based on the determination under step (i) above; (b) the transaction price under step (iii) above; (c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and (d) the contract term and pattern of satisfaction of the performance obligations under step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied.

Upfront license fees

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, manufacturing, and commercialization capabilities of the customer; the retention of any key rights by the Company; and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company exercises 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.

Customer options

The Company evaluates the customer options for material rights or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised. If an option is not exercised and the research and development target is terminated, the Company will accelerate and recognize all remaining revenue related to the material right performance obligation.

Research and development services

The promises under the Company's collaboration agreements may include research and development services to be performed by the Company for or on behalf of the customer. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts. Reimbursements from and payments to the customer that are the result of a collaborative relationship with the customer, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

Milestone payments

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved 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, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to 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.

Concentration of credit risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash and cash equivalents.

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one segment.

Cash and Cash Equivalents

The Company considers all highly-liquid investments that have maturities of three months or less when acquired to be cash equivalents. As of December 31, 2023 and 2022, cash equivalents consisted of investments in a money market account. The Company maintained $30,000 as collateral for the Company's credit card program at September 30, 2023, which was previously reported as restricted cash on its consolidated balance sheet. There were no amounts restricted as of December 31, 2023 and 2022, as the collateral was released to the Company in the fourth quarter of 2023.

Marketable Securities

The Company's marketable securities consisted of investments in U.S. Treasuries that were classified as available-for-sale. The securities were carried at fair value with the unrealized gains and losses included in accumulated other comprehensive loss, a component of stockholders' equity (deficit). Realized gains and losses and declines in value determined to be other than temporary were included in the Company's consolidated statements of operations.

Property and Equipment

Property and equipment are carried at cost less accumulated depreciation and amortization. Depreciation and amortization are calculated using the straight-line method over the estimated useful lives of the assets ranging from two to five years. Leasehold improvements are amortized over the shorter of the life of the lease or the estimated useful life of the assets. Lab equipment that are classified as finance leases are amortized over the lease term.

Long-lived Assets

Long-lived assets, such as property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. When events indicate a triggering event occurred, the recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated undiscounted future cash flows, then an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. Considerable management judgment is necessary to estimate discounted future cash flows. Accordingly, actual results could vary significantly from such estimates.

The Company did not recognize any impairment of long-lived assets during the years ended December 31, 2023 or 2022.

Deferred Financing Costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated, at which time such costs are recorded against the gross proceeds from the applicable financing. If a financing is abandoned, deferred financing costs are expensed immediately. The Company incurred $4.2 million and $4.1 million in deferred financing costs associated with the Merger during the years ended December 31, 2023 and 2022, respectively. Upon completion of the Merger, the $8.3 million of deferred financing costs were recorded against the gross proceeds received as a result of the Merger.

Leases

The Company determines whether an arrangement is or contains a lease, its classification, and its term at the lease commencement date. Leases with a term greater than one year will be recognized on the balance sheet as right-of-use (ROU) assets, current lease liabilities, and if applicable, long-term lease liabilities. The Company includes renewal options to extend the lease term where it is reasonably certain that it will exercise these options. Lease liabilities and the corresponding ROU assets are recorded based on the present values of lease payments over the lease term. The interest rate

implicit in lease contracts is typically not readily determinable. As such, the Company utilizes the appropriate incremental borrowing rates, which are the rates that would be incurred to borrow on a collateralized basis, over similar terms, amounts equal to the lease payments in a similar economic environment. Payments for non-lease components or that are variable in nature that do not depend on a rate or index are not included in the lease liability and are typically expensed as incurred. If significant events, changes in circumstances, or other events indicate that the lease term or other inputs have changed, the Company would reassess lease classification, remeasure the lease liability using revised inputs as of the reassessment date, and adjust the ROU assets. Lease expense is recognized on a straight-line basis over the expected lease term for operating classified leases.

Noncontrolling Interest

To the extent that ownership interests in the Company's subsidiary are held by entities other than the Company, management reports these as noncontrolling interests on the consolidated balance sheet. Prior to the Merger, an investor had outstanding Class B and Class B-1 shares in the Company's Luxembourg subsidiary related to the sale of the Company's Series A convertible preferred stock (Series A) and Series B convertible preferred stock (Series B). The shares were nonvoting shares at the subsidiary entity level and were presented as noncontrolling interests in the accompanying consolidated balance sheet at December 31, 2022. In connection with the Merger, the Company's noncontrolling interests exchangeable shares converted into shares of common stock (Note 8).

Research and Development Costs

Research and development costs are charged to expense as incurred. Up-front and milestone payments made to third parties who perform research and development services on the Company's behalf are expensed as services are rendered.

Stock-Based Compensation

The Company measures stock-based awards, including stock options, at their grant-date fair value and records compensation expense over the requisite service period, which is the vesting period of the awards. The Company accounts for forfeitures as they occur.

Estimating the fair value of stock options requires the use of subjective assumptions, including the fair value of the Company's common stock prior to the Merger, and, for stock options, the expected term of the option and expected stock price volatility. The Company uses the Black-Scholes option-pricing model to value its stock option awards. The assumptions used in calculating the fair value of stock options represent management's best estimates and involve inherent uncertainties and the application of management's judgment. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

Prior to the Merger, the fair value of the Company's common stock was estimated by the Company's board of directors, with input by management considering the Company's most recently available third-party valuation of the Company's common stock. The expected term of stock options for employees is estimated using the simplified method, as the Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The simplified method is the midpoint between the vesting date and the contractual term of the option. The contractual term is used as the expected term for stock options granted to nonemployees. For stock price volatility, the Company uses comparable public companies as a basis for the expected volatility to calculate the fair value of option grants. The risk-free rate is based on the U.S. Treasury yield curve commensurate with the expected term of the option. The expected dividend yield is zero given the Company does not expect to pay dividends for the foreseeable future.

Income taxes

Income taxes are accounted for under the asset and liability method. The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of the Company's assets and liabilities, and the expected benefits of net operating loss and income tax credit carryforwards. The impact of changes in tax rates and laws on deferred taxes, if any, applied during the period in which temporary differences are expected to be settled, is reflected in the Company's consolidated financial statements in the period of enactment. The measurement of deferred tax assets is reduced, if necessary, if, based on weight of the evidence, it is more likely than not that some, or all,

of the deferred tax assets will not be realized. As of December 31, 2023 and 2022, the Company has concluded that a full valuation allowance is necessary for all of its net deferred tax assets. The Company had no amounts recorded for uncertain tax positions, interest, or penalties in the accompanying consolidated financial statements. Although there are no unrecognized income tax benefits, when applicable, the Company's policy is to report interest and penalties related to unrecognized income tax benefits as a component of income tax expense.

Net loss per share

Basic net loss per share of common stock is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during each period. Diluted net loss per share of common stock includes the effect, if any, from the potential exercise or conversion of securities, such as convertible preferred stock and stock options, which would result in the issuance of incremental shares of common stock. For diluted net loss per share, the weighted-average number of shares of common stock is the same for basic net loss per share due to the fact that when a net loss exists, potentially dilutive securities are not included in the calculation as their impact is anti-dilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares of common stock outstanding, as they would be anti-dilutive:

	December 31,	
	2023	2022
Convertible preferred stock and exchangeable shares	—	9,936,148
Stock options	6,023,370	3,356,937
Conversion of convertible promissory note	—	3,258,151
	6,023,370	16,551,236

Recently adopted accounting pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326)*, which requires financial assets measured at amortized cost basis to be presented at the net amount expected to be collected. This standard is effective for fiscal years beginning after December 15, 2022. The Company adopted the guidance using a modified retrospective approach as of January 1, 2023 which resulted in no cumulative-effect adjustment to accumulated deficit and did not have a material impact on the Company's consolidated financial statements.

Recently issued but not yet adopted accounting pronouncements

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* (ASU 2023-07), which requires disclosure of incremental segment information on an annual and interim basis. This ASU is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024 on a retrospective basis. The Company is currently evaluating the effect of this pronouncement on its disclosures.

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* (ASU 2023-09), which expands the disclosures required for income taxes. This ASU is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The amendment should be applied on a prospective basis while retrospective application is permitted. The Company is currently evaluating the effect of this pronouncement on its disclosures.

(4) Merger with Sesen Bio

On March 7, 2023, Legacy Carisma completed the Merger with Sesen Bio as discussed in Note 1. The Merger was accounted for as a reverse recapitalization under GAAP because the primary assets of Sesen Bio were cash, cash equivalents and marketable securities. For financial reporting purposes Legacy Carisma was determined to be the accounting acquirer based upon the terms of the Merger and other factors, including: (i) Legacy Carisma stockholders own approximately 74.2% of the Combined Company, (ii) Legacy Carisma holds the majority (six of seven) of board seats of

the Combined Company and (iii) Legacy Carisma management holds all key positions of management. Accordingly, the Merger was treated as the equivalent of Legacy Carisma issuing stock to acquire the net assets of Sesen Bio. As a result of the Merger, the net assets of Sesen Bio were recorded at their acquisition-date fair value in the consolidated financial statements and the reported operating results prior to the Merger are those of Legacy Carisma. Immediately after the Merger, there were 40,254,666 shares of the Company's common stock outstanding.

The following table shows the net assets acquired in the Merger (in thousands):

	March 7, 2023
Cash and cash equivalents	$ 37,873
Marketable securities	44,588
Prepaid expenses and other assets	1,316
Restricted cash	30
Accounts payable and accrued expenses	(3,499)
Total net assets acquired	80,308
Less: Transaction costs	(8,264)
Total net assets acquired less transaction costs	$ 72,044

Subsequent to March 7, 2023, the Company paid $4.6 million of severance and personnel costs related to Sesen Bio.

(5) Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2023	2022
Computer software	$ 903	$ 1,062
Lab equipment[(1)]	11,392	10,260
Office furniture	267	267
Leasehold improvements	340	340
Construction in progress	13	13
	12,915	11,942
Less: accumulated depreciation and amortization[(2)]	(6,151)	(3,314)
	$ 6,764	$ 8,628

(1) Lab equipment includes failed sale lease-back assets of $3.4 million and $2.6 million, respectively, as of December 31, 2023 and 2022. Lab equipment includes finance lease ROU assets of $2.9 million as of December 31, 2023 and 2022.

(2) The accumulated amortization balance includes $0.9 million and $0.3 million, respectively, related to failed sale-leaseback assets as of December 31, 2023 and 2022. The accumulated amortization balance includes $1.7 million and $0.6 million, respectively, related to finance lease ROU assets as of December 31, 2023 and 2022.

Depreciation and amortization expense was $2.8 million and $1.9 million for the years ended December 31, 2023, and 2022, respectively.

(6) Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2023	2022
Research and development	$ 3,131	$ 4,326
Professional fees	1,366	2,100
Compensation and related expenses	3,100	2,809
Interest	—	1,126
Other	65	—
	$ 7,662	$ 10,361

(7) Commitments and Contingencies

Leases

The Company has operating leases for its laboratory and office space in Philadelphia, Pennsylvania. The Company's operating leases have term end dates ranging from 2024 to 2029. The Company also has obligations under an arrangement for the use of certain laboratory equipment that are classified as finance leases that commenced in 2022 and have end dates ranging from 2024 to 2025.

The Company's operating and finance lease right-of-use (ROU) assets and the related lease liabilities are initially measured at the present value of future lease payments over the lease term. The Company is responsible for payment of certain real estate taxes, insurance and other expenses on certain of its leases. These amounts are generally considered to be variable and are not included in the measurement of the ROU assets and lease liability. The Company accounts for non-lease components, such as maintenance, separately from lease components.

During the years ended December 31, 2023 and 2022, the Company entered into purchase and sale agreements under which the Company sold lab equipment for $1.2 million and $1.6 million, respectively. Concurrent with the sale of equipment, the Company entered into various lease agreements, with term end dates ranging from 2025 to 2026, whereby the Company will lease back the equipment. The Company accounts for such transactions as failed sale-leasebacks, due to having continuing involvement with the equipment. The Company carries this laboratory equipment as property and equipment, net on the accompanying consolidated balance sheets and the sale proceeds as a finance liability. The ongoing lease payments are recorded as reductions to the finance liability and interest expense. No gain or loss was recorded on the failed sale-leasebacks. As of December 31, 2023, the Company had a $1.9 million financing liability recorded in other current liabilities and other long-term liabilities on the consolidated balance sheets.

The elements of the lease costs were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Operating lease cost	$ 5,774	$ 4,764
Finance lease cost:		
Amortization of lease assets	1,187	560
Interest on lease liabilities	139	98
Total finance lease cost	1,326	658
Variable lease cost	1,733	920
Total lease cost	$ 8,833	$ 6,342

Lease term and discount rate information related to leases was as follows:

	December 31,	
	2023	2022
Weighted-average remaining lease term (in years)		
Operating leases	2.6	2.2
Finance leases	1.5	2.2
Weighted-average discount rate		
Operating leases	9.8%	9.4%
Finance leases	9.0%	9.0%

Supplemental cash flow information was as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash used in operating leases	$ 5,764	$ 4,750
Operating cash used in finance leases	$ 139	$ 98
Financing cash used in finance leases	$ 1,301	$ 865

Future maturities of lease liabilities were as follows as of December 31, 2023 (in thousands):

	Operating Leases	Finance Leases
Fiscal year ending:		
2024	$ 1,510	$ 600
2025	219	339
2026	226	—
2027	233	—
2028	240	—
Thereafter	184	—
Total future minimum payments	2,612	939
Less imputed interest	(361)	(67)
Present value of lease liabilities	$ 2,251	$ 872

Licensing and Sponsored Research Agreements

Under a license agreement with The Trustees of the University of Pennsylvania (Penn), entered into in November 2017 (Penn License Agreement), the Company is required to make annual payments of $25,000. Penn is eligible to receive up to $10.9 million per product in development upon the achievement of certain clinical, regulatory and commercial milestone events. There are additional milestone payments required to be paid of up to $30.0 million per product in commercial milestones and up to an additional $1.7 million in development and regulatory milestone payments for the first CAR-M product directed to mesothelin. Additionally, the Company is obligated to pay Penn single-digit royalties based on its net sales.

In March 2023, the Company entered into a manufacturing and supply agreement with Novartis Pharmaceuticals Corporation (Novartis) for the manufacturing of the Company's CT-0508 product candidate (Novartis Agreement). The Novartis Agreement is for five years and shall renew automatically for additional one-year periods unless and until

terminated by either party. In addition to paying to manufacture the product, the Company will also pay $1.0 million per calendar year, payable in quarterly payments, for reserved capacity starting on the date on which the Novartis site is declared ready to produce CT-0508 as determined by the Company. In the event of termination without cause by the Company, a termination fee equal to $4.0 million will be payable by Carisma to Novartis which, pursuant to the terms of the agreement, can be credited in full against amounts due for a substitute product.

Contingencies

Liabilities for loss contingencies, arising from claims, assessments, litigation, fines, penalties, and other sources are recorded when it is probable that a liability has been incurred and the amount of the assessment and/or remediation can be reasonably estimated.

On February 3, 2023, a purported stockholder filed a complaint in the United States District Court for the District of Delaware against Sesen Bio and its board of directors, captioned *Plumley v. Sesen Bio, Inc., et al.*, Case No. 1:23-cv-00131 (D. Del.) (the Plumley Complaint). The Plumley Complaint asserts claims under Section 14(a) of the Exchange Act and Rule 14a-9 promulgated thereunder for allegedly false and misleading statements in the proxy statement/prospectus filed as part of the Registration Statement in connection with the Merger and under Section 20(a) of the Exchange Act for alleged "control person" liability with respect to such allegedly false and misleading statements and seeks, among other relief, an order enjoining the Merger and an award for plaintiffs' fees and costs. On February 7, 2023, another purported stockholder filed a complaint in the United States District Court for the Southern District of New York against Sesen Bio and its board of directors, captioned *Franchi v. Sesen Bio, Inc., et al.*, 1:23-cv-01041 (S.D.N.Y.) (the Franchi Complaint). The Franchi Complaint contains substantially similar allegations and claims and seeks substantially similar relief as the Plumley Complaint. Additionally, on February 9, 2023, another purported stockholder filed a complaint in the United States District Court for the Southern District of New York against Sesen Bio and its board of directors, captioned *Menzer v. Sesen Bio, Inc.*, et al., 23-cv-01119 (S.D.N.Y.) (the Menzer Complaint). The Menzer Complaint contains substantially similar allegations and claims and seeks substantially similar relief as the Plumley Complaint and the Franchi Complaint. In April 2023, the Company executed a confidential fee agreement to resolve the stockholders' claim for attorney's fees and expenses in connection with the Plumley Complaint, Franchi Complaint, and Menzer Complaint. The Company settled and paid the confidential fee agreement resulting in $0.2 million of claim expenses incurred during the year ended December 31, 2023.

(8) Stockholders' Equity

On March 7, 2023, in connection with the closing of the Merger, the following is reflected on the consolidated statements of convertible preferred stock and stockholders' equity (deficit) for the year ended December 31, 2023: (i) the sale of 3,730,608 shares of common stock in a pre-closing funding at $8.21 per share for total proceeds of $30.6 million, (ii) the issuance of 5,059,338 shares of common stock upon the settlement of the Company's $35.0 million convertible promissory note, accrued interest and related derivative liability, (iii) the conversion of convertible preferred stock and exchangeable shares previously presented as noncontrolling interests into 18,872,711 shares of common stock, (iv) the issuance of 10,374,272 shares of common stock to Sesen Bio stockholders as consideration for the Merger.

On April 17, 2023, the Company filed a universal shelf registration statement on Form S-3, which was declared effective on May 2, 2023 (Registration Statement). Under the Registration Statement, the Company may offer and sell up to $300.0 million of a variety of securities, including debt securities, common stock, preferred stock, depositary shares, subscription rights, warrants and units from time to time in one or more offerings at prices and on terms to be determined at the time of the offering. On May 12, 2023, the Company entered into an Amended and Restated Open Market Sale Agreement℠ (Sale Agreement) with Jefferies LLC, as sales agent, pursuant to which the Company may offer and sell shares of common stock with an aggregate offering price of up to $100.0 million under an "at-the-market" offering program. Through December 31, 2023, the Company sold 226,533 shares for gross proceeds of $0.6 million. From January through March 2024, the Company sold an additional 931,250 shares for gross proceeds of $2.4 million.

On June 6, 2023, the Company's stockholders approved an amendment to the Company's Restated Certificate of Incorporation to increase the number of authorized shares of the Company's common stock, $0.001 par value, from 100,000,000 shares to 350,000,000 shares and authorized 5,000,000 shares of preferred stock, $0.001 par value.

(9) Stock-based Compensation

2017 Stock Incentive Plan

Legacy Carisma adopted the CARISMA Therapeutics Inc. 2017 Stock Incentive Plan, as amended (the Legacy Carisma Plan), that provided for the grant of incentive stock options to employees, directors, and consultants. The maximum term of options granted under the Legacy Carisma Plan was ten years, and stock options typically vested over a four-year period. The Company's stock options vest based on the terms in the awards agreements and generally vest over four years. Upon completion of the Merger, the Company assumed the Legacy Carisma Plan and the outstanding and unexercised options issued thereunder, and ceased granting awards under the Legacy Carisma Plan.

2014 Stock Incentive Plan

The Sesen Bio, Inc. Amended and Restated 2014 Stock Incentive Plan, as amended (the Sesen Bio 2014 Plan), provides for the grant of incentive and non-qualified stock options, restricted stock awards and restricted stock units, stock appreciation rights and other stock-based awards to the Company's employees, officers, directors, consultants, and advisors, with amounts and terms of grants determined by the Company's board of directors at the time of grant.

Stock options outstanding under the Sesen Bio 2014 Plan generally vest over a four-year period at the rate of 25% of the grant vesting on the first anniversary of the date of grant and 6.25% of the grant vesting at the end of each successive three-month period thereafter. Stock options granted under the Sesen Bio 2014 Plan are exercisable for a period of ten years from the date of grant.

On March 7, 2023, the Company amended and restated the Sesen Bio 2014 Plan to (i) change the name of the plan to the Carisma Therapeutics Inc. 2014 Amended and Restated Stock Incentive Plan (the 2014 Plan) and (ii) adopt a new form of stock option agreement and a new form of restricted stock unit agreement for the grant of options and restricted stock units under the 2014 Plan. On June 6, 2023, the Company's stockholders approved an amendment and restatement of the Company's 2014 Plan, which amendment and restatement had previously been adopted by the Company's board of directors, subject to stockholder approval. As of December 31, 2023, approximately 4.9 million shares of common stock remained available for issuance.

2014 Employee Stock Purchase Plan

The Sesen Bio 2014 Employee Stock Purchase Plan (the Sesen Bio 2014 ESPP) provides employees with the opportunity to purchase shares of common stock at a 15% discount to the market price through payroll deductions or lump sum cash investments. The purpose of the Sesen Bio 2014 ESPP is to enhance employee interest in the success and progress of the Company by encouraging employee ownership of common stock. On March 7, 2023, the Company amended and restated the Sesen Bio 2014 ESPP to (i) change the name of the plan to Carisma Therapeutics Inc. 2014 Employee Stock Purchase Plan and (ii) restate and integrate all prior amendments thereto. As of December 31, 2023, 0.2 million shares of common stock remained available for issuance.

The following table summarizes stock option activity for the year ended December 31, 2023:

	Options	Weighted average exercise price	Weighted average remaining contractual term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	3,356,937	$ 1.01		
Sesen Bio options assumed in the Merger	765,223	27.94		
Exercised	(128,716)	1.29		$ 134
Granted	2,984,152	6.93		
Forfeited	(114,454)	5.80		
Expired	(839,772)	29.48		
Outstanding as of December 31, 2023	6,023,370	$ 3.94	7.8	$ 5,929
Exercisable as of December 31, 2023	2,516,594	$ 1.16	6.0	$ 4,950
Vested and expected to vest at December 31, 2023	6,023,370	$ 3.94	7.8	$ 5,929

The weighted-average grant-date per share fair values of options granted during the year ended December 31, 2023 and 2022 were $4.29 and $1.46, respectively. The fair values in the year ended December 31, 2023 and 2022 were estimated using the Black-Scholes option-pricing model based on the following assumptions:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	2.92% - 4.76%	2.40% - 3.05%
Expected term	6 years	6 years
Expected volatility	57.77% - 103.00%	54.54% - 56.50%
Expected dividend yield	—	—

Stock-Based Compensation Expense

The Company recorded stock-based compensation expense in the following expense categories in the accompanying consolidated statements of operations:

	Year Ended December 31,	
	2023	2022
Research and development	$ 1,242	$ 143
General and administrative	1,074	132
	$ 2,316	$ 275

The Company recognized stock-based compensation expense of $0.2 million related to the modification of Sesen Bio options assumed in connection with the Merger. Compensation cost for awards not vested as of December 31, 2023 was $11.2 million and will be expensed over a weighted-average period of 3.3 years.

(10) Income Taxes

A reconciliation of income tax benefit at the statutory federal income tax rate and income taxes as reflected in the consolidated financial statements is as follows:

	Year Ended December 31,	
	2023	2022
Federal tax benefit at statutory rate	(21.0) %	(21.0) %
State and local tax, net of federal benefit	(8.5)	(7.8)
State and local tax rate change	1.6	6.2
Permanent differences	0.4	2.0
Research and development	(0.9)	(2.9)
Change in valuation allowance	28.4	22.4
Return to provision	—	1.1
Total provision	— %	— %

Deferred tax assets and liabilities are determined based on the differences between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which differences are expected to reverse.

Significant components of the Company's deferred tax assets for federal income taxes consisted of the following (in thousands):

	December 31,	
	2023	2022
Deferred tax assets		
Net operating losses	$ 72,689	$ 27,021
Capitalized research and development costs, net of amortization	33,778	11,907
Research and development credits	9,746	5,643
Start-up costs	4,407	4,744
Deferred revenue	13,353	—
Lease liability	668	1,451
Amortizable assets and other	21	59
Equity compensation	87	74
Gross deferred tax assets	134,749	50,899
Valuation allowance	(133,580)	(49,105)
Deferred tax assets, net of valuation allowance	1,169	1,794
Deferred tax liabilities		
Right of use asset	(645)	(1,430)
Depreciation	(524)	(364)
Deferred tax liabilities	(1,169)	(1,794)
Net deferred tax assets and liabilities	$ —	$ —

As of December 31, 2023, the Company has net operating loss carryforwards (NOLs) for federal income tax purposes of $317.6 million, which are available to offset future federal taxable income. The pre-2018 federal NOLs of $120.0 million will begin to expire in 2037, if not utilized. The post-2017 federal NOLs of $197.6 million carry forward indefinitely. The Company also has NOLs for state and local income tax purposes of $229.4 million and $40.8 million, respectively that are available to offset future taxable income. The state NOLs will begin to expire in 2038 while the city of Philadelphia NOLs expire after three years with $29.7 million expiring in 2023. As of December 31, 2023, the Company also had federal and state research and development tax credit carryforwards of $9.9 million that will begin to expire in 2029, unless previously utilized.

In assessing the need for a valuation allowance, management must determine that there will be sufficient taxable income to allow for the realization of deferred tax assets. Based upon the historical and anticipated future losses, management has determined that the deferred tax assets do not meet the more-likely-than-not threshold for realizability. Accordingly, a full valuation allowance has been recorded against the Company's net deferred tax assets as of December 31, 2023. The valuation allowance increased by $84.5 million and $13.7 million during the years ended December 31, 2023 and 2022, respectively.

The NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOLs and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percent, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not done an analysis to determine whether or not ownership changes have occurred since inception. Certain state NOLs may also be limited, including Pennsylvania, which limits net operating loss utilization as a percentage of apportioned taxable income.

The Company will recognize interest and penalties related to uncertain tax positions as a component of income tax expense/(benefit). As of December 31, 2023, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's financial statements. Tax years from 2019 and after remain subject to examination by all of the taxing jurisdictions. The NOLs and research credit carryforwards remain subject to review until utilized.

(11) Related-Party Transactions

The Company has a collaboration and license agreement with Moderna, a significant shareholder (Note 12).

(12) Moderna Collaboration and License Agreement

In January 2022, the Company entered into the Moderna License Agreement, which provides for a broad strategic collaboration to discover, develop and commercialize *in vivo* engineered CAR-M therapeutics for up to twelve oncology programs. Under the Moderna License Agreement, the Company and Moderna initiate research programs during a research term, focused on the discovery and research of products directed to biological targets. Moderna’s mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Moderna has the right to designate up to twelve research targets as development targets. The first five research targets have been designated and all programs are currently in the discovery phase. Moderna funds the cost of the Company's activities in accordance with an agreed research budget. The Company is responsible for discovering and optimizing development candidates, and Moderna is responsible for the clinical development thereafter. Pursuant to the Moderna License Agreement, the Company and Moderna formed a joint steering committee (JSC) that is responsible for the coordination and oversight of all research activities to which the Company is responsible for providing. The JSC is comprised of representatives from the Company and Moderna and with Moderna having final decision-making authority, subject to specified limitations.

During the term of the Moderna License Agreement, the Company and its affiliates are subject to various exclusivity obligations under which the Company is not permitted to research, develop or commercialize particular products outside of the collaboration, including products for use as *in vivo* therapies in the field of oncology, products directed to any target included in the collaboration, or products containing a polypeptide provided by the Company to Moderna in connection with a research program that are directed to any development target. Additionally, the Company has granted Moderna an exclusive worldwide royalty free license to the Company’s intellectual property associated with the product candidates that permits Moderna to conduct its research and development activities. Upon Moderna’s election of a development target (and payment of a related development target designation milestone) for commencement of pre-clinical development of a product candidate, the Company will grant Moderna an exclusive worldwide, sublicensable royalty bearing license to develop, manufacture and commercialize the product candidate.

Under the terms of the Moderna License Agreement, Moderna made an upfront non-refundable payment of $45.0 million to the Company. Assuming Moderna develops and commercializes 12 products, each directed to a different development target, the Company is eligible to receive up to between $247.0 million and $253.0 million per product in development target designation, development, regulatory and commercial milestone payments. Moderna also will reimburse the Company for all costs incurred by the Company in connection with its research and development activities under the Moderna License Agreement plus a reasonable margin for the respective services performed (with a minimum commitment to reimburse $10.0 million in research and development costs over the first three years from execution of the Moderna License Agreement). The Company is also eligible to receive tiered mid-to-high single digit royalties of net sales of any products that are commercialized under the agreement, which may be, subject to reductions. In addition, Moderna has agreed to cover the cost the Company incurs for certain milestone payments royalties the Company owes as a licensor under one of its intellectual property in-license agreements with Penn that the Company is sublicensing to Moderna under the Moderna License Agreement, which royalties Moderna may deduct in part from any royalties owed to the Company. The Moderna License Agreement terminates on a product-by-product basis upon the latest of expiration of the applicable product patents, expiration of regulatory exclusivity and the tenth anniversary of first commercial sale, unless terminated earlier by the Company or Moderna.

At commencement, the Company identified several potential performance obligations within the Moderna License Agreement, including research and development services on research targets, option rights held by Moderna, a non-exclusive royalty-free license to use the Company's intellectual property to conduct research and development activities and participation on the JSC. The Company determined that there were 2 performance obligations comprised of (i) research and development services and (ii) option rights.

For the research and development services, the stand-alone selling price was determined considering the expected passthrough costs and cost of the research and development services and a reasonable margin for the respective services. The material rights from the option rights were valued based on the estimated discount at which the option is priced and the Company's estimated probability of the options' exercise as of the time of the agreement. The transaction price allocated to research and development services is recognized as collaboration revenues as the research and development services are provided to satisfy the underlying obligation related to the research and development target. The transfer of control occurs over this period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation.

The transaction price of $45.0 million allocated to the options rights, which are considered material rights, will be recognized in the period that Moderna elects to exercise or elects to not exercise its option right to license and commercialize the underlying research and development target.

The Company included the $45.0 million up-front and nonrefundable payment and $73.9 million of variable consideration for expected research and development services to be performed during the five-year contract term, inclusive of passthrough costs, in the transaction price as of the outset of the arrangement. During the year ended December 31, 2023 and 2022, the Company recognized $14.9 million and $9.8 million, respectively, of research and development services as collaboration revenues as the Company is the principal in providing such services. The Company recognized $24.7 million of collaboration revenues since inception of the Moderna License Agreement through December 31, 2023. The following table includes estimated revenue expected to be recognized in the future related to performance obligations that are unsatisfied as of December 31, 2023 (in thousands):

	Transaction price unsatisfied
Performance obligations:	
Research and development	$ 49,183
Option rights	45,000
Total performance obligations	$ 94,183

Amounts due to the Company for satisfying the revenue recognition criteria or that are contractually due based upon the terms of the collaboration agreements are recorded as accounts receivable in the Company's consolidated balance sheets. Contract liabilities consist of amounts received prior to satisfying the revenue recognition criteria, which are recorded as deferred revenue in the Company's consolidated balance sheets.

The following table summarizes the changes in deferred revenue (in thousands):

	Year Ended December 31,	
	2023	2022
Balance at the beginning of the period	$ 47,459	$ —
Deferral of revenue	13,873	57,293
Recognition of unearned revenue	(14,919)	(9,834)
Balance at the end of the period	$ 46,413	$ 47,459

The current portion of deferred revenue represents advanced payments received from Moderna for costs expected to be incurred by the Company within the next twelve months. The noncurrent portion of deferred revenue represents the $45.0 million upfront, non-refundable and non-creditable payment allocated to customer option right which is not expected to be recognized within the next 12 months.

(13) Subsequent Events

The Company has evaluated subsequent events from the balance sheet date through April 1, 2024, the issuance date of these consolidated financial statements, and has not identified any additional matters requiring disclosure.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer has evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as of December 31, 2023. The term "disclosure controls and procedures," as defined in the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2023, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were 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 our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with the authorizations of management and directors; and

- provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, our management concluded that our internal control over financial reporting were effective as of December 31, 2023.

Changes in Internal Control over Financial Reporting

No changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Director and Officer Trading Arrangements

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the fourth quarter of 2023.

Strategic Evaluation and Cost Reduction Measures

On March 27, 2024, in connection with an assessment of appropriate expense reduction efforts, our board of directors approved an expense reduction plan, which included a reduction in workforce, in order to extend the Company's cash runway, reduce operating expenses and further align our workforce with expense allocation on our assets with the greatest strategic interest. Affected employees were informed of the reduction in workforce on or about April 1, 2024. The reduction in workforce represents approximately 39 full-time employees (representing approximately 37% of our total workforce), including certain employees engaged in research and development activities and certain finance and corporate employees. We expect to incur approximately $2.1 million in connection with the reduction in workforce, which primarily represents one-time employee termination benefits directly associated with the workforce reduction. We expect the reduction in workforce to be substantially complete and to pay the majority of these reduction in workforce amounts in the second quarter of 2024. The estimate of costs that we expect to incur, and the timing thereof, are subject to a number of assumptions and actual results may differ. We may also incur other charges or cash expenditures not currently contemplated due to events that may occur as a result of, or associated with, the reduction in workforce.

Director Resignation

On March 27, 2024, Chidozie Ugwumba notified us of his decision to resign from our board of directors, effective April 1, 2024. At the time of his resignation, Mr. Ugwumba was a member of the audit committee. Mr. Ugwumba decided to resign from our board of directors as a result of his other professional commitments and not due to a disagreement on any matter related to our operations, policies or practices.

Effective April 1, 2024, Michael Torok will become the Chair of the audit committee. Following Mr. Ugwumba's resignation, the audit committee is now comprised of Michael Torok (Chair), Regina Hodits, Ph.D., and Sanford Zweifach.

Director Appointment

On March 27, 2024, our board of directors elected John Hohneker, M.D. as a director of the Company, effective as of April 1, 2024. Dr. Hohneker was appointed as a Class I director and will serve in accordance with our amended and restated by-laws until our 2024 annual meeting of stockholders and thereafter until his successor is duly elected and qualified or until his earlier death, resignation or removal. Dr. Hohneker will serve on the nominating and corporate governance and science committees.

In accordance with our non-employee director compensation policy, Dr. Hohneker will receive (i) annual cash compensation of $40,000 for his service as a director and an additional cash retainer for any committees on which he serves and (ii) reimbursement for reasonable out-of-pocket business expenses incurred in connection with attending meetings of our board of directors and committees thereof. In addition, in accordance with our non-employee director compensation policy, Dr. Hohneker was granted a stock option under the Carisma Therapeutics Inc. 2014 Amended and Restated Stock Incentive Plan to purchase 38,700 shares of our common stock at a per share exercise price equal to the closing price of our common stock on April 1, 2024, the date of grant. The option will vest as to 2.7778% of the shares of our common stock underlying the option at the end of each successive one-month period over a three-year period following the date of grant, subject to continued service with the company.

In connection with his election, we and Dr. Hohneker will enter into our standard form of indemnification agreement, a copy of which is filed as Exhibit 10.8 to this Annual Report on Form 10-K. Pursuant to the terms of the indemnification agreement, we may be required, among other things, to indemnify Dr. Hohneker for certain expenses and costs relating to claims, suits or proceedings arising out of his service as a director of the company. There are no arrangements or understandings between Dr. Hohneker and any other person regarding his election to the board of directors and Dr. Hohneker does not have a direct or indirect material interest in any related party transaction required to be disclosed under Item 404(a) of Regulation S-K.

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

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance.

Except to the extent provided below, the information required under this Item 10 is incorporated by reference to our definitive proxy statement for our 2024 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2023.

We post our Code of Business Conduct and Ethics, which applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in the "Governance Overview" sub-section of the "Governance" section of our corporate website at *http://www.carismatx.com*. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required under this Item 11 is incorporated by reference to our definitive proxy statement for our 2024 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2023.

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

The information required under this Item 12 is incorporated by reference to our definitive proxy statement for our 2024 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2023.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this Item 13 is incorporated by reference to our definitive proxy statement for our 2024 Annual Meeting of Stockholders, which proxy statement we intend to file with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year ended December 31, 2023.

Item 14. Principal Accounting Fees and Services.

The information required under this Item 14 is incorporated by reference to our definitive proxy statement for our 2024 Annual Meeting of Stockholders, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the end of the fiscal year ended December 31, 2023.

Part IV

Item 15. Exhibits and Financial Statement Schedules.

1. **Financial Statements**

For a list of financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K.

2. **Financial Statement Schedules**

All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

3. **Exhibits**

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of Carisma Therapeutics Inc., dated March 7, 2023 (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
3.2	Amended and Restated By-Laws of Carisma Therapeutics Inc., dated March 7, 2023 (incorporated by reference to Exhibit 3.2 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
3.3	Certificate of Amendment to Restated Certificate of Incorporation of Carisma Therapeutics Inc., dated June 6, 2023 (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on June 9, 2023).
10.1#	Amendment and Restatement of Carisma Therapeutics Inc. Amended and Restated 2014 Stock Incentive Plan (incorporated by reference to Exhibit 99.1 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on June 9, 2023).
10.2†	Amended and Restated Open Market Sale Agreement[SM], dated May 12, 2023 (incorporated by reference to Exhibit 1.1 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on May 12, 2023).
10.3†	Collaboration and License Agreement, dated January 7, 2022, by and between Carisma and ModernaTX, Inc. (incorporated by reference to Exhibit 10.32 to the Registrant's Registration Statement on Form S-4/A (File No. 333-267891), filed on January 18, 2023).
10.4†	License Agreement, dated as of November 10, 2017, by and between Carisma and the Trustees of the University of Pennsylvania, as amended (incorporated by reference to Exhibit 10.33 to the Registrant's Registration Statement on Form S-4 (File No. 333-267891), filed on October 14, 2022).
10.5†	License Agreement, dated as of July 24, 2020, by and between Carisma and New York University (incorporated by reference to Exhibit 10.34 to the Registrant's Registration Statement on Form S-4 (File No. 333-267891), filed on October 14, 2022).
10.6	Registration Rights Agreement, dated March 7, 2023 (incorporated by reference to Exhibit 10.4 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.7	Contingent Value Rights Agreement, dated March 7, 2023 (incorporated by reference to Exhibit 10.5 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.8	Form of Indemnification Agreement for Directors and Officers of Carisma Therapeutics Inc. (incorporated by reference to Exhibit 10.6 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).

10.9#	Employment Agreement, dated March 7, 2023, by and between Carisma Therapeutics Inc. and Steven Kelly (incorporated by reference to Exhibit 10.7 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.10#	Employment Agreement, dated March 7, 2023, by and between Carisma Therapeutics Inc. and Richard Morris (incorporated by reference to Exhibit 10.8 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.11#	Employment Agreement, dated March 7, 2023, by and between Carisma Therapeutics Inc. and Michael Klichinsky (incorporated by reference to Exhibit 10.9 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.12#	CARISMA Therapeutics Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.10 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.13#	Form of Nonstatutory Stock Option Agreement under the CARISMA Therapeutics Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.11 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.14#	Form of Incentive Stock Option Agreement under the CARISMA Therapeutics Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.12 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.15#	Carisma Therapeutics Inc. Amended and Restated 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.13 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.16#	2023 Form of Stock Option Agreement under the Carisma Therapeutics Inc. 2014 Amended and Restated Stock Incentive Plan (incorporated by reference to Exhibit 10.14 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.17*	2024 Form of Stock Option Agreement under the Carisma Therapeutics Inc. 2014 Amended and Restated Stock Incentive Plan.
10.18#	Form of Restricted Stock Unit Agreement under the Carisma Therapeutics Inc. 2014 Amended and Restated Stock Incentive Plan (incorporated by reference to Exhibit 10.15 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.19#	Carisma Therapeutics Inc. 2014 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.16 to the registrant's Current Report on Form 8-K (File No. 001-36296) filed on March 8, 2023).
10.20	Lease, dated April 22, 2019, by and between Wexford-SCEC 3675 Market Street, LLC and CARISMA Therapeutics Inc. (incorporated by reference to Exhibit 10.18 to the registrant's Quarterly Report on Form 10-Q (File No. 001-36296) filed on May 11, 2023).
21.1*	Subsidiaries of the Registrant
23.1*	Consent of KPMG LLP, independent registered public accounting firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1+	Certifications of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2+	Certifications of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
97*	Compensation Recovery Policy
101.INS*	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its 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 (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

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* Filed herewith.

\+ Furnished herewith.

\# Indicates a management contract or any compensatory plan, contract or arrangement.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

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, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: April 1, 2024

CARISMA THERAPEUTICS INC.

By: /s/ Steven Kelly
Name: Steven Kelly
Title: President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Steven Kelly Steven Kelly	President, Chief Executive Officer and Director (Principal Executive Officer)	April 1, 2024
/s/ Richard Morris Richard Morris	Chief Financial Officer (Principal Financial and Accounting Officer)	April 1, 2024
/s/ Sanford Zweifach Sanford Zweifach	Director and Chair of the Board	April 1, 2024
/s/ Regina Hodits, Ph.D. Regina Hodits, Ph.D.	Director	April 1, 2024
/s/ Briggs Morrison, M.D. Briggs Morrison, M.D.	Director	April 1, 2024
/s/ Björn Odlander, M.D. Björn Odlander, M.D.	Director	April 1, 2024
/s/ Michael Torok Michael Torok	Director	April 1, 2024
/s/ Chidozie Ugwumba Chidozie Ugwumba	Director	April 1, 2024