# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

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

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

**OR**

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

**Commission File Number 001-40629**

# CANDEL THERAPEUTICS, INC.

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

| **Delaware** | **52-2214851** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **117 Kendrick St, Suite 450 Needham, MA** | **02494** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (617) 916-5445**

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

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, par value $0.01 per share | CADL | The Nasdaq Global Market |

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of voting stock held by non-affiliates of the registrant on June 30, 2022, based on the closing price of $3.24 for shares of the registrant's common stock as reported by the Nasdaq Global Market, was approximately $72.3 million. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purposes.

The number of shares of registrant's Common Stock outstanding as of March 15, 2023 was 28,919,810.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 Annual Meeting of Stockholders (the Proxy Statement) are incorporated by reference in Part III of this Annual Report on Form 10-K. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after

the end of the fiscal year to which this report relates. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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## Forward-Looking Statements

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, product candidates, clinical development plans and expectations, prospective products, product approvals, research and development costs, timing and likelihood of success, and plans and objectives of management for future operations and results, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the risks, uncertainties and assumptions described under the sections in this Annual Report titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” These forward-looking statements are subject to numerous risks, including, without limitation, the following:

- the timing and the success of preclinical studies and clinical trials of CAN-2409 and CAN-3110 and any other product candidates;
- the initiation of any clinical trials of CAN-2409 and CAN-3110 and any other product candidates;
- our need to raise additional funding before we can expect to generate any revenues from product sales;
- our ability to conduct successful clinical trials or obtain regulatory approval for CAN-2409 and CAN-3110 or any other product candidates that we may identify or develop;
- the ability of our research to generate and advance additional product candidates;
- the effects of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations;
- our ability to establish an adequate safety or efficacy profile for CAN-2409, CAN-3110 or any other product candidates that we may pursue;
- our ability to manufacture CAN-2409, CAN-3110 or any other product candidate in conformity with our specifications and the U.S. Food and Drug Administration’s (FDA) requirements and to scale up manufacturing of our product candidates to commercial scale, if approved;
- the implementation of our strategic plans for our business, any product candidates we may develop and any companion diagnostics;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates any companion diagnostics;
- the rate and degree of market acceptance and clinical utility for any product candidates we may develop;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the period we estimate to be funded by our existing financial resources;
- our ability to establish and maintain collaborations;
- the potential benefits with the continued existence of our license agreement with Mass General Brigham (MGB);
- our financial performance;
- our ability to effectively manage our anticipated growth;
- developments relating to our competitors and our industry, including the impact of government regulation; and
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements

may not occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, new risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances, or otherwise.

You should read this Annual Report and the documents that we reference in this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify that all of our forward-looking statements by these cautionary statements.

All references to "Candel", "we", "us", "our", or the "Company" mean Candel Therapeutics, Inc. and its subsidiary.

**Summary of the Material and Other Risks Associated with Our Business**

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

- We are a biopharmaceutical company with a limited operating history and we have not generated any revenue from product sales. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years and may never achieve or maintain profitability.
- We will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.
- We have incurred indebtedness, and we may incur additional indebtedness, which could adversely affect our financial condition.
- Our business is dependent on the success of our lead product candidate, CAN-2409, as well as CAN-3110 and any other product candidates that we advance into the clinic. All of our product candidates will require additional development before we may be able to seek regulatory approval for and launch a product commercially.
- Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent or delay development, regulatory approval, and commercialization.
- Our product candidates are based on a novel approach to the treatment of cancer, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval, if at all.
- Even if we receive marketing approval for our current or future product candidates, our current or future product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.
- The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or experience delays in obtaining, required regulatory approvals, we will not be able to commercialize CAN-2409, CAN-3110 and future product candidates as expected, and our ability to generate revenue may be materially impaired.
- The FDA’s agreement to a Special Protocol Assessment with respect to the study design of our Phase 3 clinical trial of CAN-2409 in newly diagnosed localized prostate cancer in intermediate and high-risk patients does not guarantee any particular outcome from regulatory review, including ultimate approval, and may not lead to a successful review or approval process.
- Some of our product candidates are being and may continue to be studied in third-party research and clinical trials sponsored by organizations or agencies other than us, or in investigator-sponsored clinical trials, which means we will have minimal or no control over the conduct of such trials and which may adversely affect our ability to obtain marketing approval or certain regulatory exclusivities.
- Changes in product candidate manufacturing or formulation may result in additional costs or delay.

- The COVID-19 pandemic, which began in late 2019 and has spread worldwide, may affect our ability to complete our ongoing clinical trials and initiate and complete other preclinical studies, planned clinical trials or future clinical trials, disrupt regulatory activities, disrupt our manufacturing and supply chain, or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.
- If the government or third-party payors fail to provide adequate coverage, reimbursement and payment rates for our product candidates, or if health maintenance organizations or long-term care facilities choose to use therapies that are less expensive or considered a better value, our revenue and prospects for profitability will be limited.
- If the manufacturers upon which we may rely fail to produce our product candidates in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to biopharmaceutical manufacturers, we may face delays in the development and commercialization of, or be unable to meet demand for, our product candidates and may lose potential revenues.
- The transition of our manufacturing operations to a third-party contract manufacturer may result in further delays or expenses, and we may not experience the anticipated operating efficiencies.
- Our rights to develop and commercialize certain of our product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

## PART I

### Item 1. Business.

#### Overview

We are a clinical stage biopharmaceutical company focused on developing and commercializing viral immunotherapies to help patients fight cancer. Our engineered viruses are designed to induce a systemic anti-tumor response due to immunogenic cell death through direct viral-mediated cytotoxicity in cancer cells, thus releasing tumor neo-antigens and creating a pro-inflammatory microenvironment. Our viral immunotherapy approach utilizes intratumoral administration of genetically engineered viruses to induce tumor cell death and elicit a systemic anti-tumor response. Local delivery enables us to achieve these effects while aiming to minimize systemic toxicity. The immune cells induced by these viral immunotherapies are believed to target patients' specific tumor antigens, potentially improving responses in immunologically "hot" tumors while at the same time infiltrating the tumor microenvironment, transforming non-inflamed "cold" tumors with limited immune response into "hot" tumors. While our product candidates are administered directly into the tumor, we have observed a systemic immune response in our preclinical studies and clinical trials that may indicate the potential of our product candidates to induce a systemic immune response against distal, uninjected tumors, also known as an "abscopal" effect.

We believe viral immunotherapy is among the most promising cancer treatment modalities today. Our goal is to further improve patient outcomes through viral immunotherapies by selecting the optimal vector, specific transgenes and clinical indications for each tumor type while optimizing product candidate attributes, such as high-titer formulation, intratumoral administration to induce systemic anti-tumor immunity, and storage conditions that could potentially lower logistical barriers for patients and clinicians.

We have established two clinical stage viral immunotherapy platforms based on novel, genetically modified adenovirus and herpes simplex virus (HSV) constructs, respectively.

Our most advanced product candidate, CAN-2409, is an off-the-shelf adenovirus product candidate which is combined with the prodrug, valacyclovir, that has generated promising clinical activity across a range of solid tumor indications. CAN-2409 is currently being studied in the following ongoing clinical trials:

- *Prostate Cancer*
  - a Phase 3 randomized, triple-blinded and placebo-controlled clinical trial in the United States under a Special Protocol Assessment (SPA), with the U.S. Food and Drug Administration (FDA) evaluating 711 patients with newly diagnosed, localized prostate cancer who have an intermediate or high-risk for progression. We completed enrollment of this trial in September 2021 and we expect to present topline data at the end of 2024.
  - a Phase 2 randomized, double blind, placebo-controlled clinical trial in the United States evaluating 187 patients with low-to-intermediate risk localized prostate cancer undergoing active surveillance. We completed enrollment of this trial in May 2019 and we expect topline data from this clinical trial to be available in the fourth quarter of 2024.
- *Non-small Cell Lung Cancer (NSCLC)* – an open-label Phase 2 clinical trial in the United States evaluating CAN-2409 plus valacyclovir in combination with continued PD-(L)1 checkpoint inhibitors in 80 patients with stage III/IV NSCLC who have inadequate response to PD-(L)1 checkpoint inhibitors. We reported initial data from this trial at the American Society for Clinical Oncology (ASCO) Annual Meeting in June 2022 and an update during our Research and Development Day in December 2022, demonstrating the following:
  - Evidence of local and systemic anti-tumor activity
  - Disease control rate of 77% (20/26) in patients entering trial with disease progression (cohort 2)
  - Sustained and ongoing clinical responses greater than 1 year
  - Favorable change in trajectory of tumor progression
  - Decreased tumor size of RECIST target lesions in most patients
  - Reduced uninjected tumor size in 14/21 patients (67%)
  - Overall response rate of 13% (4/30) across cohorts 1 and 2
  - Durable disease stabilization translating into encouraging preliminary evidence of progression-free survival
  - Consistent induction of local and systemic cytotoxic T cell response
  - Increased infiltration of CD8+ T cells in the tumor microenvironment
  - Systemic expansion of effector T cells and increase in soluble granzyme B levels in peripheral blood
  - Favorable safety/tolerability data with most treatment-related adverse events being grade 1/2

We anticipate presenting additional updated clinical data from this ongoing clinical trial in the third quarter of 2023.

- *Pancreatic Cancer* – we have initiated a randomized Phase 2 clinical trial in the United States evaluating CAN-2409 in borderline resectable pancreatic adenocarcinoma. In March 2023, in connection with our cost management and dynamic portfolio management initiatives, we paused new enrollment in this randomized Phase 2 clinical trial, subject to additional funding. Despite the pause in patient enrollment, we continue to expect to present initial clinical data in the fourth quarter of 2023. In a previous Phase 1b trial, patients with pancreatic cancer treated with CAN-2409 in addition to standard of care demonstrated a greater survival duration over the expected survival of the patients treated with the existing standard of care alone in a comparison to historical trial results. Furthermore, in the group of patients where pre- and post-treatment tumor biopsies were available, a statistically significant increase in the number of CD8+ tumor infiltrating lymphocytes was observed.

Our lead HSV-based product candidate, CAN-3110, is currently in an ongoing investigator-sponsored Phase 1 clinical trial in our initial target indication of recurrent high-grade glioma (HGG). These patients have failed standard of care treatment and have a poor prognosis. Initial clinical data from this trial was presented in an oral presentation at the ASCO Annual Meeting in June 2021, and additional biomarker data was reported in November 2021. During our Research and Development Day in December 2022, we presented updated data demonstrating that CAN-3110 was well tolerated with no observed dose-limiting toxicity, achieved 11.6 months mOS with a single dose, and showed evidence of persistent HSV-1 antigen and HSV-1 replication consistent with mechanism of action as well as robust evidence of immune activation.

We are currently evaluating the effects of multiple doses of CAN-3110 in recurrent HGG supported by the Break Through Cancer foundation.

We are also designing other novel viral immunotherapy candidates using our proprietary enLIGHTEN™ Discovery Platform, the first systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics to create new viral immunotherapy candidates for solid tumors. In October 2022, we entered into a collaboration with the University of Pennsylvania (UPenn) Center for Cellular Immunotherapies to study the impact of novel viral immunotherapy candidates based on Candel's enLIGHTEN™ Discovery Platform to strengthen the activity of UPenn's investigational CAR-T cell therapies in difficult to treat solid tumors.

We currently own development and commercialization rights for our programs in major markets, including the United States, Europe and Asia, allowing us to control development and seek approval in those areas as we prepare our commercialization efforts.

We were incorporated in Delaware in June 2003 as Advantagene, Inc. (Advantagene). In December 2019, Advantagene licensed substantially all the assets of Periphagen, a company focused on engineering HSV as a gene therapy vector, and in September 2020, licensed CAN-3110 from Mass General Brigham (MGB). In December 2020, we formally changed our name from Advantagene to Candel Therapeutics, Inc. We completed our initial public offering in July 2021.

**Our Strategy**

Our goal is to develop best-in-class viral immunotherapies to transform the lives of cancer patients. We plan to develop and commercialize our two lead product candidates, CAN-2409 and CAN-3110, for the treatment of a broad range of solid tumor indications, while continuing to build our pipeline through our discovery platform. Key elements of our strategy include the following:

- *Advance the late-stage development of, and seek regulatory approval for, our lead product candidate, CAN-2409, in newly diagnosed, localized prostate cancer.* We are currently conducting a potentially registrational Phase 3 clinical trial in intermediate- and high-risk patients in combination with the standard of care, radiotherapy. If approved, we believe CAN-2409 could be a first-in-class drug for localized prostate cancer patients with the potential to reduce disease progression and recurrence.
- *Advance the clinical development of CAN-3110 from our HSV platform with tumor-specific enhanced replication potency.* An investigator-sponsored Phase 1 clinical trial is ongoing in recurrent HGG. This trial is evaluating the activity of CAN-3110 in therapy-resistant disease, where we believe a replicating virus may present therapeutic advantages.
- *Advance the development of CAN-2409 in stage III/IV NSCLC patients with inadequate responses to standard of care immune checkpoint inhibitors (ICI).* A Phase 2 trial that evaluates CAN-2409 in combination with ICI is currently underway in NSCLC.
- *Continue to expand the development of CAN-2409 in other solid tumor indications, such as pancreatic cancer.* We believe we can leverage our broad clinical experience to expand the development of CAN-2409

in other indications. We have initiated a randomized Phase 2 clinical trial in patients with borderline resectable pancreatic adenocarcinoma. However, in March 2023, in connection with our cost management and dynamic portfolio management initiatives, we elected to pause new enrollment in this randomized Phase 2 clinical trial, subject to additional funding.

- *Leverage our HSV viral immunotherapy platform to develop additional HSV-based product candidates.* Our new enLIGHTEN™ Discovery Platform enables rapid vector engineering to generate a range of new candidates in a data driven and indication specific manner. We utilize a key attribute of HSV, a high capacity for genetic cargo, to seek to enable targeted modifications and deploy indication specific genes to the tumor microenvironment. Our platform is designed to generate both replication-defective and replication-competent agents depending on the demands of a particular application.
- *Establish strategic partnerships to maximize the value of our current and future product candidates.* In order to advance treatment options for a large number of patients, we may partner with other companies with complementary resources to maximize the value of our current and future product candidates. Such partnerships may allow us to pair CAN-2409, CAN-3110 and our future product candidates with other novel agents owned by strategic partners. Partnerships may also help realize the full potential of our product candidates in markets where we are unlikely to pursue development or commercialization on our own. We intend to maintain significant economic interest in our product candidates and selectively consider partnership opportunities.
- *Ensure commercial-scale manufacturing of our product candidates.* We will rely on third party contract manufacturers for commercial-scale manufacturing of our adenovirus product candidate, CAN-2409. We expect that our cost-of-goods will be substantially lower than cell- and antibody-based therapies because of our high-yield manufacturing process.

**Our Approach**

Conventional cancer therapies (chemotherapy, radiotherapy and surgery) often do not eradicate 100% of the tumor cells, which often leads to tumor progression or recurrence. Deep and durable responses, therefore, are still elusive for many cancer patients. Traditionally, surgery and/or radiotherapy are used for local tumor debulking, whereas chemotherapeutic agents target systemic eradication of tumor cells. These treatment modalities, however, are often limited by toxicity.

Immunotherapy is a relatively new treatment modality that has expanded the anti-cancer treatment paradigm. FDA-approved immunotherapies include cytokines, cell therapies and antibodies, including ICIs. Much focus has been placed on harnessing the effector T cell arm of the immune system for tumor specific immunity. Adoptive T cell therapy has shown positive results but with limited activity in solid tumors, and is not scalable for widespread use. Vaccine approaches range in complexity from peptide antigens to autologous or allogeneic tumor cell products. The advantage of the single antigen approaches is that they can be easily manufactured and produced, however, they have the fundamental disadvantage of being potentially irrelevant for a patient's specific tumor or immune system or easily bypassed by resistant clones. Cellular vaccines are not easily scalable and allogeneic vaccines may not bear the relevant antigens expressed by a patient's tumor. ICIs such as anti-PD-1 and anti-PD-L1 antibodies, have transformed the treatment paradigm for different cancer indications. However, only approximately 15% to 40% of overall patients respond to such treatment.

We are focused on the development of viral immunotherapy approaches, which are based on an extensive history of research. Originally, the mechanism of action of those agents was believed to be based only on the ability of the virus to induce cancer cell lysis and to resolve tumors. Later, it was demonstrated that viral immunotherapy may induce immunogenic cell death. This effect may be enhanced by the pro-inflammatory effects of the viral capsid proteins. With the dramatic emergence of ICIs and immunotherapy as a core treatment modality, the importance of the immunostimulatory aspect of viral-mediated approaches became more widely evident. The currently understood generalized mechanism of action of viral immunotherapies is unique in combining both an anti-tumor cytotoxic component and an immune-stimulatory component. Together, these modalities lead to an "in-situ vaccination" effect against the injected tumor followed by an effect on uninjected distant metastases.

Pairing this therapeutic approach with ICI treatment or with radiotherapy is based on a strong mechanistic rationale and has shown promise in experimental models of cancer. It has been observed that tumors that are least responsive to ICI are commonly characterized by low levels of lymphocytic infiltration and low or no PD-L1 expression levels; they are referred to as "cold" tumors. One of our areas of focus is the conversion of immunologically suppressed "cold" tumors into immunologically active "hot" tumors, thereby increasing their responsiveness to ICI or other therapies, such as radiotherapy.

***The Mechanism of Action of Viral Immunotherapy:***

- *Direct anti-tumor cytotoxic activity.* Tumor-specific viral-mediated oncolysis is achieved by both precise delivery of the engineered virus to the tumor as well as the virus' ability to selectively replicate within a cancer cell. Various approaches have been applied in different programs to increase the specificity and potency of viral toxicity aimed at tumor cells, including genetic modifications and use of prodrugs.
- *Broad stimulation of anti-tumor immunity.* The immunogenic cell death driven by oncolysis results in a potent local and systemic immune stimulation with the increased expression of proinflammatory cytokines, chemokines and adhesion molecules. This, in turn, promotes the activation of both the innate and adaptive arms of the immune system in the presence of highly immunogenic viral components. This broad response commonly includes recruitment and activation of antigen-presenting cells and effector immune cells to the site of the tumor.
- *Priming of the immune system against tumor antigens.* The lysis of cancer cells leads to the exposure of tumor-specific antigens. This early effect, combined with intratumoral immune cell infiltration and activation, leads to antigen presentation and initiation of a local adaptive immune response targeted against a set of tumor antigens expressed by the patient's cancer cells.
- *Development of a systemic immune memory response.* Viral immunotherapy induces the development of a long-lasting systemic immune surveillance against the antigens associated with the injected tumor, and consequently, tumor antigens expressed at metastatic sites. This leads to a cytotoxic immune response against the distant tumor cells, also known as an abscopal effect.

***Desirable Clinical Properties.*** Viral immunotherapy has attributes that are important for a cancer therapeutic. The agents are off-the-shelf, and while they have been shown to stimulate immune responses in most patients, there is no requirement to modify them for each patient, unlike other cellular therapy approaches. The first viral immunotherapy was approved by the FDA in 2015, providing support that additional agents in this class may have similar potential. Furthermore, safety data shown in several clinical trials of various immunotherapies supports the ability to combine viral immunotherapy with other agents due to the potential for fewer overlapping side effects.

***Our Immunotherapy Platforms.*** Our two platforms, one based on adenovirus and the other based on HSV, provide different and complementary sets of attributes, which allows us to utilize the product candidate that is best suited for a particular clinical application.

Key attributes across our viral immunotherapy platforms include:

- *Targeting a Wide Range of Cell Types.* Product candidates from both the HSV and adenoviral platforms can transduce a diverse range of cell types, which we believe will allow us to address many different forms of cancer.
- *Off-the-Shelf Product.* A standardized product intended to be available as needed via prescription supports straightforward clinical administration, simplified manufacturing and supply chain management.
- *Intratumoral Route of Administration.* Both of our product candidates are administered by direct injection into the tumor site. This aims to maximize immune stimulation and minimize systemic toxicity, factors that are believed to be suboptimal with intravenous administration. We believe that directly injecting these viral immunotherapies into a patient's cancerous tissue helps to optimize the benefit/risk for these agents to be highly immunostimulatory at the site of the tumor, whereas systemically administered agents would need to avoid detection by the body's immune surveillance mechanisms to avoid rapid destruction before getting to the target tumor. While our product candidates are administered directly into the tumor, we have observed a systemic immune response in our preclinical studies and clinical trials that may indicate the potential of our product candidates to induce systemic immune response against distal, uninjected tumors, also known as an "abscopal" effect. For the indications that we selected, intratumoral administration is a straightforward procedure that is aligned with clinical practice, leveraging standard of care medical procedures, such as intra-prostate injection or delivery during diagnostic (bronchoscopy) or therapeutic (neurosurgery) procedures.
- *Cost-efficient Manufacturing.* Both product candidates are relatively inexpensive to manufacture, particularly when compared to other biologic or cellular therapy treatments.

Key attributes of our Adenoviral platform include:

- *Targeting a Wide Range of Cell Types.* Adenoviruses can efficiently transduce cells from different lineages. This allows us to apply this platform to many different tumor types.
- *Immunogenic Virus Particle.* The adenoviral virus particles are strong simulators of the innate immune system, a property that contributes to immune activation at the site of administration.

- *High-Titer Formulation.* Adenovirus can be formulated at high titers, facilitating the administration of low volume doses sufficiently potent to induce strong activity.
- *Product Stability.* The formulation deployed in clinical trials has stability at refrigerator temperatures (4°C), supporting use at less specialized and therefore widely accessible sites such as community-based private clinics.
- *Non-Replicating Design*. Engineering the adenovirus to remove replication ability reduces the potential for viral shedding, something which is particularly important in clinical applications such as prostate cancer. There is no need for *in vivo* amplification as the virus is highly immunogenic and can be administered at high titers.

Key attributes of our CAN-3110 platform include:

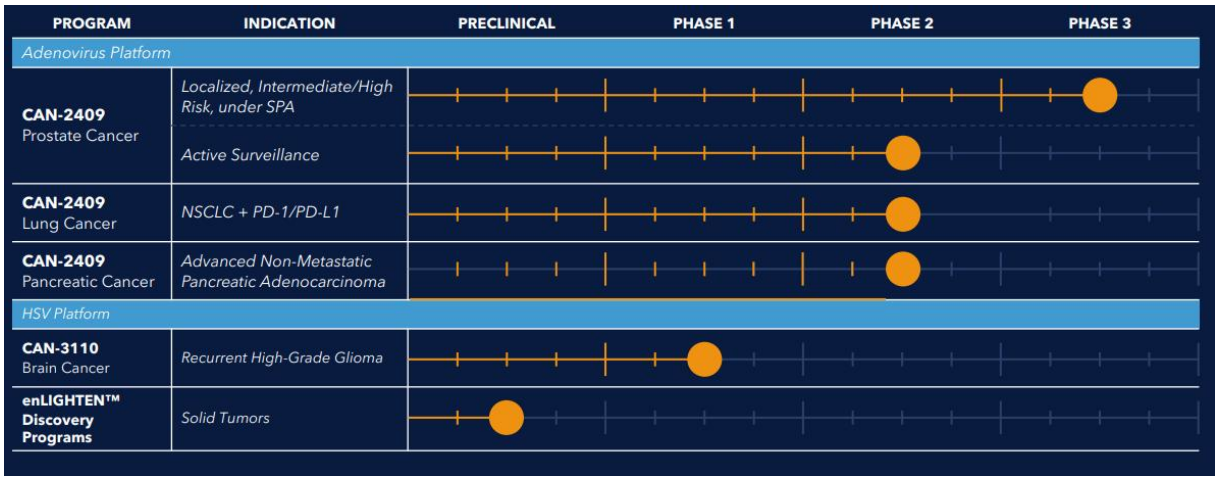
- *Capacity for selective replication in the tumor.* There is a strong rationale for use of a replication-competent virus that is designed to provide potent oncolysis and viral amplification in tumors characterized by high volume or located in less anatomically accessible areas, such as recurrent HGG. We have engineered CAN-3110 to selectively replicate only within tumors. This tumor specific replication ability of CAN-3110 is regulated by the expression of ICP34.5, a gene encoding for a protein that permits viral replication even in the presence of the interferon response that is normally able to quell viral infection. In the CAN-3110 construct, ICP34.5 expression is driven by the expression of Nestin, a protein largely expressed in certain tumors, like gliomas, but not in healthy brain tissue, thereby enabling replication specifically in the context of brain tumors. We believe our HSV-based platform will allow us to implement additional genetic modifications to leverage the use of CAN-3110 in recurrent HGG and in other tumor types expressing Nestin.
- *Oncolytic activity combined with immunostimulatory properties.* CAN-3110 is designed to persist and replicate at the site of the tumor. Viral replication is accompanied by tumor oncolysis, with release of tumor antigens in the microenvironment and activation of local systemic immune response.

Key attributes of the enLIGHTEN™ Discovery Platform include:

- *Strong focus on human biology, including deep phenotyping of human tumors, to increase probability of success*
- *Data driven selection of the payload.* The use of advanced analytics on proprietary and publicly available datasets enables us to select what we believe is the best payload for combinatory strategy in a specific indication, rationalizing our payload selection, de-risking development and maximizing our probability of success.
- *Use of HSV based on its high capacity for genetic cargos*. Our HSV-based platform allows the introduction of large genetic cargos, such as multiple immunomodulatory genes that may further enhance the anti-tumor immune response.
- *Amenable to engineered modifications.* Our knowledge of virus biology allows us to make modifications, such as those already present in CAN-3110 to target certain tumor types. Leveraging these modifications, we can select the best viral vector to deliver the selected payload in a specific indication.

**Our Pipeline**

We have an advanced pipeline of late-stage and early-stage clinical trials with our two lead product candidates, CAN-2409 and CAN-3110.




CAN-2409, formerly known as gene mediated cytotoxic immunotherapy (GMCI), is our most advanced product candidate. It is a replication defective adenovirus that has been genetically modified to express the gene encoding the HSV-thymidine kinase enzyme. This enzyme activates the prodrug, valacyclovir, a widely available, generally well-tolerated antiviral at the site of the tumor, generating a powerful patient-specific anti-tumor immune response. We believe there are three key aspects of the mechanism of action. First, the direct, cellular killing activity is based on the transformation of valacyclovir into a toxic nucleotide analogue that disrupts DNA synthesis and repair. This phenomenon occurs preferentially in actively dividing cancer cells, thereby providing tumor specificity. This DNA repair inhibition is also hypothesized to be the mechanistic explanation behind the encouraging pre-clinical and clinical activity of CAN-2409 in combination with radiotherapy, a treatment known to cause DNA breaks requiring repair for continued cellular survival. Second, adenoviral capsid proteins themselves also directly trigger an immuno-inflammatory response through the establishment of a proinflammatory tumor microenvironment, resulting in the expression of proinflammatory cytokines, chemokines, and adhesion molecules that contribute to the optimal conditions to immunize against the tumor antigens that are released in the tumor microenvironment as a direct result of the formed toxic nucleotide analogues. Together, this results in the recruitment, activation and proliferation of anti-tumor effector cells, in particular CD8+ cytotoxic T cells. Consequently, the localized death of tumor cells releases numerous antigens that can be recognized by the patient's own immune system, thereby training the immune system to recognize, target and destroy cancer cells bearing the same antigens that have spread to other sites in the body.

To date, CAN-2409 has been administered to over 950 patients with cancer, who are in ongoing, placebo-controlled randomized trials. In total, we have conducted more than 10 clinical trials with CAN-2409 in a range of solid tumor indications. We have seen encouraging clinical activity and a favorable tolerability profile with CAN-2409 in both monotherapy and combination settings with radiotherapy, ICI therapy, androgen deprivation therapy (ADT), chemotherapy and surgery. Based on the totality of our clinical data generated to date, we are currently pursuing indications in lung, pancreatic, and prostate cancer, which we believe all have great potential to address unmet need.

We are conducting a Phase 3 clinical trial with CAN-2409 under agreement with the FDA through the SPA process in newly diagnosed localized prostate cancer in intermediate- and certain high-risk patients in combination with the standard of care that comprises radiotherapy and optional ADT. Our SPA provides FDA concurrence that our key endpoints and specific critical elements of our trial design are adequate to support a future marketing application if, among other things, we achieve the primary endpoint in the trial. The clinical trial is randomized, triple-blinded and placebo-controlled. It targeted enrollment of approximately 700 patients and was fully enrolled with 711 patients in September 2021 with topline data anticipated at the end of 2024. We have also received fast track designation by the FDA for the development of CAN-2409 for the treatment of localized, primary prostate cancer in combination with radiotherapy to improve the local control rate, decrease recurrence and improve disease-free survival. We expect that if the trial is successful and if we obtain FDA approval, CAN-2409 could be the first new FDA approved pharmacologic treatment available in over 30 years as a first-line therapeutic for the over 100,000 patients who are newly diagnosed with localized prostate cancer each year in the United States.

We have also completed enrollment for a Phase 2 clinical trial with CAN-2409 as monotherapy in newly diagnosed prostate cancer patients under active surveillance. This trial has recruited 187 patients with low-, intermediate- and certain high-risk localized prostate cancer. We expect to announce topline data in the fourth quarter of 2024. We believe that this trial, if successful, could position CAN-2409 as a first-line monotherapy treatment for patients with low- and intermediate-risk prostate cancer, thereby meaningfully expanding the addressable patient population.

In NSCLC, we have observed monotherapy activity of CAN-2409 in a Phase 1 biomarker focused, window of opportunity clinical trial. In 2020, we initiated a Phase 2 clinical trial evaluating CAN-2409 in combination with PD-(L)1 checkpoint inhibitors for patients with inadequate response to PD-(L)1 ICI. This open label trial, as amended, is targeting enrollment of approximately 80 patients with stage III/IV NSCLC in two separate cohorts. The cohorts are defined based on response to ICI at the time of enrollment. Cohort 1 addresses patients with stable disease at enrollment. Cohort 2 enrolls patients with progressive disease after at least 18 weeks of ICI treatment. Patients will continue treatment with their initial checkpoint inhibitor and CAN-2409 will be added to their regimen. The primary efficacy endpoint for this trial is tumor response as measured by RECIST criteria including overall response rate (ORR) and/or disease control rate (DCR). We reported initial data from this trial at the ASCO Annual Meeting in June 2022 and during our Research and Development Day in December 2022, we presented updated data showing evidence of local and systemic anti-tumor activity; a DCR of 77% (20/26) in patients entering the trial with disease progression (cohort 2); sustained and ongoing clinical responses greater than 1 year; favorable change in the trajectory of tumor progression; decreased tumor size of RECIST target lesions in most patients; reduced uninjected tumor size in 14/21 patients (67%); an overall response rate of 13% (4/30) across cohorts 1 and 2; durable disease stabilization translating into encouraging preliminary evidence of progression-free survival; consistent induction of local and systemic cytotoxic T cell response; increased infiltration of CD8+ T cells in the tumor microenvironment; systemic expansion of effector T cells and increase in soluble granzyme B levels in the peripheral blood; and a favorable safety/tolerability data with most treatment-related adverse events being grade 1/2. We anticipate presenting additional updated data from this ongoing clinical trial in the third quarter of 2023.

We have initiated a randomized Phase 2 clinical trial evaluating CAN-2409 in borderline-resectable pancreatic adenocarcinoma. In March 2023, in connection with our cost management and dynamic portfolio management initiatives, we elected to pause new enrollment in this randomized Phase 2 clinical trial, subject to additional funding. Despite the pause in patient enrollment, we continue to expect to present initial clinical data in the fourth quarter of 2023. In a previous Phase 1b trial, patients with pancreatic cancer treated with CAN-2409 in addition to standard of care demonstrated a greater survival duration over the expected survival of the patients treated with the existing standard of care alone in a comparison to historical trial results. Furthermore, in the group of patients where pre- and post-treatment tumor biopsies were available, a statistically significant increase in the number of CD8+ tumor infiltrating lymphocytes was observed.

Our second viral immunotherapy platform is based on a novel, next generation, genetically modified HSV that induces tumor specific oncolysis. The HSV-based platform enables generation of both replication-competent and replication-defective viral product candidates as well as capacity to clone, in the vector, up to five transgenes that will allow us to optimize our virus profile for different tumor settings. CAN-3110, our first HSV-based product candidate, has been engineered for enhanced specificity and tumor cell killing, while minimizing toxicity on healthy tissue. CAN-3110 was formerly known as rQNestin34.5v.2. An investigator-sponsored Phase 1 clinical trial is ongoing with CAN-3110 in our initial target indication of recurrent HGG and we reported additional biomarker results in November 2021. During our Research and Development Day in December 2022, we presented updated data demonstrating that the treatment was well tolerated, with no observed dose-limiting toxicity; produced a median overall survival (mOS) of 11.6 months with a single dose; showed evidence of immune activation and persistent HSV-1 antigen and HSV-1 replication consistent with the mechanism of action. We are currently evaluating the effects of multiple doses of CAN-3110 in recurrent HGG supported by the Break Through Cancer foundation. Based on the molecular targeting of CAN-3110, we believe that it could be evaluated in an expanded range of indications in the future, such as other neurologic tumors, melanoma, gastrointestinal stromal tumors, thyroid tumors and breast cancer.

In addition, we are pursuing novel discovery programs based on our enLIGHTEN™ Discovery Platform.

**Market Opportunity**

The four indications where we have the most advanced clinical trials are localized prostate cancer, NSCLC, pancreatic cancer, and recurrent HGG. These types of cancer present substantial market opportunities and are also enabling indications for future expansion into other solid tumors.

***Localized Prostate Cancer***

Prostate cancer is the second leading cause of cancer deaths in men in the United States, representing a high level of medical burden and unmet need. The prostate cancer therapy market is estimated to grow to over $16.1 billion by 2026. Approximately 200,000 men in the United States are diagnosed with prostate cancer annually, with more than 30,000 deaths each year. Although most deaths occur in patients with later stage metastatic disease, most prostate cancer patients roughly 150,000 annually in the United States are initially diagnosed in the early stage of disease, of which roughly 105,000 are considered to have intermediate- or high-risk of progression and approximately 45,000 are considered to be low-risk.

For the intermediate- and high-risk patients, the standard of care is radical prostatectomy and radiotherapy often in conjunction with androgen deprivation therapy or chemical castration. These treatments have a high incidence of

potentially life altering side effects, including incontinence and erectile dysfunction. There is therefore a significant unmet need for a novel treatment able to forestall or prevent progression to later stages of disease without the burdensome side effects associated with the current standard of care. Weighing the balance between therapeutic efficacy and side effects linked to therapy, about 10% of the intermediate-risk patients, and approximately 40% of the low-risk patients decide, in consultation with their physicians, to adopt a close monitoring approach known as active surveillance that involves periodic imaging, biomarker evaluation and biopsies. Standard of care in this early, localized setting, leaves substantial need unaddressed.

As a result of PSA screening programs, most patients are diagnosed at early stages of disease with low grade, low volume, asymptomatic prostate cancer. Current screening methods are inadequate to definitively identify which patients are most likely to progress. As a result of these side effects, there is a large desire to delay or prevent the need for radical treatment. As a result, many men with prostate cancer meeting the National Comprehensive Cancer Network (NCCN) guidelines for low-risk prostate cancer choose not to be treated and to undergo an intense monitoring program, known as Active Surveillance (AS), as their preferred initial course of treatment. However, within 10 years of diagnosis, between 21% and 38% of men will have developed progressive cancer and require invasive treatments. It has been reported that 21% and 41% of patients initially under AS convert to active treatment based on progression of their disease within two and five years, and approximately 17% of men undergoing AS choose to move to active treatments within 10 years of diagnosis, even in the absence of any evidence of progression, underscoring the level of concern around progression and the significant unmet need in this early line of treatment.

To our knowledge, the only FDA-approved pharmacologic intervention indicated for newly diagnosed localized prostate cancer is chemical castration therapy, also known as ADT. Standard of care for localized disease is primarily surgery, radiotherapy and/or ADT. Because ADT has a potentially severe side effect profile, including impotence, hot flashes, mood changes, depression and others, these hormone treatments are reserved only for those patients that present the highest risk of localized or metastatic prostate cancer. Similarly, surgical prostatectomy can often cause urinary dysfunction and sexual dysfunction that can last years and sometimes be permanent. Approximately one-third of men with normal baseline function will report some increase in urinary symptoms and urgency after prostatectomy and most men will experience some erectile dysfunction after treatment with either surgery or radiation.

We believe CAN-2409 provides a significant commercial opportunity for therapeutic use in the newly diagnosed, localized prostate cancer patient population, with the goal of reducing progression or recurrence of disease without significant toxicities and with a product that can be administered at outpatient facilities.

***Non-Small Cell Lung Cancer***

In recent years ICI, specifically PD-1 directed agents, have transformed the treatment paradigm of NSCLC and become a backbone therapy for this indication. Over a half dozen ICI products have been approved in various cancer indications, and there are numerous other related drug candidates in preclinical and clinical development. Global sales for ICIs in 2019 were approximately $23 billion with NSCLC accounting for 50% to 55% of overall sales. The commercial opportunity in NSCLC is significant. Drug treated patient populations in the US for 2020 are estimated at 75,160; 47,920 and 21,990 in first-, second- and third-line treatment, respectively. ICI use in NSCLC has become standard of care with approximately 49% of first-line patients in the United States being treated with an ICI alone or in combination with other agents. Nonetheless, 60% of these patients will have an inadequate response after one year of ICI treatment, and 80% after three years.

***Pancreatic Cancer***

The American Cancer Society estimates that approximately 64,050 people in the United States (33,130 men and 30,920 women) will be diagnosed with pancreatic cancer in 2023; about 50,550 people (26,620 men and 23,930 women) will die of pancreatic cancer this year. Treatment is with surgery in cases where tumors are resectable, followed by adjuvant chemoradiation; there is increasing use of neoadjuvant chemoradiation in borderline resectable or even resectable disease in order to better reduce the risk of recurrence. For resected patients, while surgery and adjuvant approaches (e.g. FOLFORINOX) have improved median overall survival, 5 year survival rates remain modest (20-30%) and most tumors will recur (median recurrence free survival ~1.5 years). While there is a high level of total clinical research and development activity across pancreatic cancer settings (over 150 investigational products in Phase 2 or later development), the majority are targeting metastatic disease. Physicians have identified a continued unmet need for more effective treatment options across the pancreatic cancer setting, including a need for further approaches which can increase the resectability of borderline / locally advanced patients, and improving cure rates in resected patients. There are an estimated 18,510 patients with resectable disease, with a sizeable proportion receiving surgery and adjuvant therapy; there are 12,340 patients with borderline resectable disease and 30,850 with locally advanced tumors (with the majority undergoing neoadjuvant / induction treatment) in the US/EU5.

***High-Grade Glioma***

Glioblastoma, the most common form of HGG, is a relatively rare cancer with first-line drug treated prevalent population in the United States of approximately 16,113 patients. Treatment in the upfront setting is surgical resection, if possible, coupled with temozolomide and/or radiotherapy; however, virtually all patients eventually develop recurrent disease.

The prognosis for glioblastoma that has recurred is dire; median overall survival with second line chemotherapy such as lomustine is associated with median overall survival of 6-9 months. Few pharmaceutical treatment options exist for patients with recurrent HGG, with the last significant FDA approval over a decade ago. Avastin was approved in 2009, specifically for patients with recurrent glioblastoma, and approval was granted despite the absence of a survival benefit in the registrational studies. New agents to treat patients with recurrent HGG are urgently needed.

**Our Product Candidates**

***Lead Product Candidate - CAN-2409***

We believe the adenovirus-based CAN-2409 has advantageous properties that differentiate from other viral immunotherapies. Namely, CAN-2409:

- *Has consistently shown activity in clinical trials across a range of solid tumor types.*
- *Has been dosed in hundreds of patients and has generated favorable tolerability and safety data.*
- *Is engineered to be potently immunogenic but non-replicating with the goal of maximizing the anti-tumor immune response while minimizing the risk for local and systemic toxicity.*
- *Can be stored at 4°C, facilitating the use of CAN-2409 in out-patient clinics. This aspect is particularly favorable in indications such as prostate cancer, where patients are often monitored in individual private practices.*

CAN-2409 (international non-proprietary name: aglatimagene besadenovec) is an adenovirus-based replication-defective engineered gene construct encoding the thymidine kinase gene derived from the herpes simplex virus. It is injected directly into the tumor or target tissue. Localized injection is intended to minimize systemic toxicities associated with systemic intravenous administration, eliminating the requirement for complex immune evasion or tumor-specific targeting mechanisms, and focuses the immune response locally against the tumor, while also activating the desired systemic anti-tumoral response against the injected tumor and uninjected metastases. The adenoviral vector is used to transport the thymidine kinase gene into the tumor cells at the site of injection. HSV-thymidine kinase converts generic, FDA-approved anti-herpes drugs, such as ganciclovir, acyclovir and valacyclovir, which we use as prodrugs, into a toxic nucleotide analogue. These agents are widely available, inexpensive and are generally well-tolerated. Cells transduced with the thymidine kinase gene as well as neighboring cells that are replicating or exhibit DNA damage undergo immunogenic cell death after exposure to these systemically administered prodrugs that are converted in the tumor microenvironment into toxic metabolites.

The prodrug-derived cytotoxic nucleotide analogs are designed to inhibit DNA replication and repair, leading to the death of multiplying tumor cells, and in particular of cells undergoing repair from radiation or chemotherapy damage. This form of cell death is immunogenic and exposes tumor antigens that can elicit a further tumor-specific immune response. Additionally, the virus itself stimulates a marked immuno-inflammatory response. Key pro-inflammatory cytokines as well as chemokines, adhesion molecules and costimulatory molecules are locally upregulated, resulting in an inflamed (hot) tumor microenvironment, able to further enhance CD8+ cytotoxic T cell activation and immunization against released tumor antigens.

This local effect provides a strong mechanistic rationale for the combination of viral immunotherapy with ICIs such as PD-1 or PD-L1 targeting antibodies. ICI agents work by unmasking the inhibitory signals provided by PD-L1 ligands on tumor cells when bound to PD-1 receptors on T cells. By blocking this suppressive signal pharmacologically, it has been demonstrated that T cells can be unleashed to attack cancer cells and that profound clinical benefit can be achieved, but this benefits only a minority of patients. It has been hypothesized that treatment results can be significantly improved by optimizing recognition of the specific tumor antigens by the patient's adaptive immune system using viral immunotherapy combined with the non-specific stimulation of T cells induced by ICI treatment. It appears that a duality of signals is required: releasing the checkpoint inhibition as described earlier, coupled with the provision of a positive, stimulatory signal to T cells. The efficient presentation of tumor specific antigens by MHC class I molecules to the immune system provides just such a specific, stimulatory signal. Viral immunotherapies have been shown to facilitate such cross presentation of tumor antigens and are therefore an attractive complement to PD-1 or PD-L1 checkpoint blockade.

The immune system is highly dynamic, with continuous trafficking of different populations of immune cells throughout the body. One outcome of this is that when T cells are locally activated and trained to recognize tumor-specific antigens, they can act systemically to drive an efficient immune response at sites distant from the original tumor. This abscopal effect may explain the significant effects observed at distant, uninjected sites demonstrated in experimental models of cancers. Abscopal effect has been shown with CAN-2409 in a mouse model of prostate cancer. The model employed

RM-1, a syngeneic prostate cell line, that was implanted both in the flanks of the mice as well as systemic, via a tail vein injection to mimic metastatic disease, resulting in the emergence of lung tumor nodules. After intratumor treatment of the flank tumor masses with either CAN-2409 and systemic prodrug, alone or in combination with radiotherapy, we observed a beneficial response in both injected and uninjected metastatic tumor. Use of CAN-2409 resulted in a 38% mean reduction in tumor volume and, in the combination arm, a reduction of 61% in tumor volume. Notably, the average number of lung nodules was reduced from 20.5 in the control arm and 22.4 in the mice that received radiotherapy to 13.0 in the CAN-2409 arm, and to 6.6 when CAN-2409 was combined with radiotherapy. We have also observed the abscopal response in connection with the experimental treatment of CAN-2409 in patients with NSCLC.

The activity of CAN-2409 treatment has been shown to be dependent on CD8+ T cell involvement in studies in mouse models that evaluated permutations of CAN-2409 treatment and T cell depletion. Furthermore, T cells from mice that were successfully treated with CAN-2409 and prodrug were shown to be sufficient to inhibit tumor growth when mixed with AKR tumor model cells and implanted subcutaneously in mouse flanks. This activity was not observed with T cells from untreated mice, from mice that were treated with a control vector that lacked the thymidine kinase gene, or when the AKR tumor cells were xenografted alone. These data are consistent with a T cell dependent mechanism of action of CAN-2409. Additionally, we have shown the induction of CD8+ T cell infiltration at the site of the tumor in patients with prostate cancer, pancreatic cancer, and NSCLC.

***Second Product Candidate - CAN-3110***

CAN-3110 is a modified HSV with specific properties that can be leveraged in diverse clinical indications. Namely, CAN-3110:

Is engineered to provide oncolysis through replication specifically in Nestin expressing cancer cells.

- *Has demonstrated statistically significant survival benefit in preclinical models of brain cancer.*
- *Has generated favorable tolerability and safety data, not reaching a dose limiting toxicity in the dose range tested in an ongoing investigator-sponsored Phase 1 trial.*
- *Has shown a clinical signal in a difficult to treat brain cancer population, critically defined by a highly immunosuppressive environment.*
- *Has been engineered to replicate in a range of other indications characterized by Nestin expression.*
- *Is derived from our HSV-based platform that also provides the potential to support expansion of our pipeline with novel agents.*

CAN-3110 is an engineered HSV where the expression of ICP34.5, the gene responsible for viral replication, has been placed under the control of a tumor-specific Nestin promoter. Nestin is a cytoskeletal protein that is overexpressed in glioma cells, but it is absent in the healthy adult brain. In CAN-3110, ICP34.5 expression is controlled by the Nestin promotor enabling viral replication selectively in tumor cells. This replication-competent HSV construct provides tumor-specific cytolytic activity, while sparing healthy cells that do not express Nestin.

This modification of the viral genome of CAN-3110 enables us to maintain the function of ICP34.5, an HSV protein that allows virus replication even in the presence of a suppressive interferon response, under strict control and only in tumor cells.

ICP34.5 is deleted in other HSV oncolytic viruses that may be less tumor selective with an intent of achieving a favorable safety profile, which may result in viruses characterized by poor replication ability and a limited ability to generate an effective anti-tumor immune response.

**Our Clinical Trials**

***CAN-2409 for Prostate Cancer***

We have completed multiple Phase 1 and Phase 2 clinical trials in non-metastatic prostate cancer using CAN-2409 as monotherapy and in combination with standard of care. These trials generated favorable tolerability and safety data and also provide evidence to support CAN-2409 immune activation, dosing levels and schedules. We have administered CAN-2409 to about 900 patients with localized prostate cancer to date, most of whom are currently in ongoing, placebo-controlled randomized trials.

*Monotherapy Activity*

We have observed what we believe to be a clinical response with CAN-2409 as monotherapy in our Phase 1 trials. These responses have been consistently observed in patients with prostate cancer, including patients with newly diagnosed, localized disease, as well as those whose cancer was progressing even after radiotherapy.

In newly diagnosed patients with localized prostate cancer, analysis of biopsies following monotherapy CAN-2409 treatment revealed change in glandular architecture, necrosis and increased immune cell infiltration as compared to baseline biopsy. We observed in treated samples a 4-fold increase in the number of CD8+ T cells and a 3-fold increase in the number of CD68+ macrophages, demonstrating immune response after CAN-2409 administration.

In another Phase 1/2 clinical trial, patients whose prostate cancer had progressed following radiotherapy and that presented a persistently rising PSA level, were treated with CAN-2409 as monotherapy using six dose levels, ranging from $1x10^8$–$1x10^{11}$ viral particles. In 27 of the 36 patients recruited, a decrease in PSA levels was observed following a single cycle of CAN-2409, as measured by the best PSA decrease in serial assessments within the first 3 months after treatment. PSA, while an imperfect biomarker for prostate cancer, is still widely employed for patient management in conjunction with biopsy, as rising PSA levels, and in particular PSA doubling time are associated with disease progression. In that same trial, we observed that the PSA doubling time improved significantly (p=0.0271) from 15.9 months at baseline to 42.5 months after a single cycle of CAN-2409 administration, in this treatment resistant patient population. A subset of the patients in this trial also received second or third injection courses of CAN-2409. In most of those patients, a decrease from pre-administration PSA levels was again observed upon repeated injection.

*Combination Therapy*

Because of the increasing prevalence of combination therapy for cancer patients, the ability to combine novel agents with standard of care treatments without overlapping toxicity is of increasing importance. We believe that the favorable tolerability and safety data generated for CAN-2409 in our clinical trials is encouraging for our current and future development plans, in combination with other agents but also as a monotherapy in lower risk patient populations that are not willing to undergo more aggressive forms of treatment. The safety data from our Phase 2 clinical trial in prostate cancer patients treated with CAN-2409 in combination with standard of care of radiotherapy or androgen deprivation therapy, reported no grade 4 treatment-related adverse events and only single-patient incidence of grade 3 treatment related adverse events. It was anticipated that flu-like symptoms would be evident, because CAN-2409 is an adenoviral gene construct known to induce a systemic immune response. Greater than 50% of patients reported fever and/or chills often associated with viral immune activation. These symptoms, which generally manifested early and transiently, often occurred on the evening of the intratumoral administration of CAN-2409 and resolved by the following morning. The rates of the gastrointestinal adverse events are consistent with those typically reported by patients undergoing radiotherapy, which is a component of standard of care in this population.

Our previous Phase 2 clinical trial data informed our agreement with the FDA under the SPA for our ongoing Phase 3 clinical trial. Although the data is limited as we have not conducted head-to-head studies, in our Phase 2 clinical trial we observed that intermediate-risk patients who received CAN-2409 in combination with radiotherapy had failure rates that were 75% lower than those reported in four other contemporaneous trials of similar patient populations. Where these other clinical trials reported freedom from failure rates of between 75%-79%, corresponding to cumulative recurrence rates of 21%-25%, CAN-2409 resulted in a 5% recurrence rate in patients with intermediate-risk prostate cancer. The median follow-up of patients who received CAN-2409 in this clinical trial was 5.7 years. Similarly, results in this clinical trial also demonstrated reduced recurrence rates in the low- and high-risk patients enrolled when compared to these other trials. Furthermore, a pathological complete response (pCR) was observed in 93% of the biopsies available at 2yrs (37%-73% in control populations). In this trial, low-risk patients achieved a PSA of < 2ng/ml in 77% of CAN-2409 treated patients versus 58% in control populations.

The endpoint used in our Phase 2 trial was freedom from failure (FFF), defined by the period of time between treatment and the occurrence of a clinical or biochemical failure. Under the SPA agreement, we have selected disease-free survival (DFS) as the endpoint for our Phase 3 clinical trial. The DFS definition requires an objective detection of tumor progression. This largely overlaps with FFF as it is often triggered by detection of increased PSA levels (i.e., biochemical failure). We have also reanalyzed our previous Phase 2 data using DFS parameters, supporting the implementation of DFS as endpoint in our Phase 3 trial.

*Potentially Registrational Phase 3 Clinical Trial for Localized Prostate Cancer*

We are developing CAN-2409 as a potential therapeutic option that avoids the long-term severe side effects of hormone therapy or surgical interventions. Based on the data from our clinical trials to date, we believe that CAN-2409 has the potential, if approved, to be the first new first-line product candidate approved for patients with localized prostate cancer in over 30 years. We are currently conducting a potentially registrational Phase 3 trial for CAN-2409, with agreement, under an SPA with the FDA for a single pivotal trial in newly diagnosed localized prostate cancer in intermediate and high-risk patients in combination with the standard of care, radiotherapy.

This Phase 3 clinical trial is fully enrolled with 711 patients, randomized 2:1. Patients receive three investigational treatment courses of CAN-2409, each consisting of four concurrent injections of transrectal ultrasound guided administration of CAN-2409 followed by a course of oral valacyclovir. The first injection course is given at least 15 days but not more than 8 weeks before starting radiation. The second injection course is given 0-3 days prior to radiotherapy. The third and final injection course is delivered 15-22 days after the second injections. A fixed dose of valacyclovir is

given for 14 days after each CAN-2409 administration. Standard of care external beam radiotherapy is administered to patients throughout the course of the trial with optional ADT as determined by the treating physician.

Trial inclusion criteria are based on patients with localized prostate cancer meeting the NCCN criteria of intermediate-risk or patients presenting only one NCCN high-risk feature. NCCN intermediate-risk is defined as having at least one of the following: prostate serum antigen (PSA) of 10-20 ng/ml, Gleason Score of 7, and is staged T2b-T2c via the TNM staging system. Patients may also exhibit one high-risk characteristic that may consist of a PSA of 20+ ng/ml, a Gleason Score of 8-10, or a cancer that is up to stage T3a, but not more than one of these high-risk factors.

The SPA agreement specifically defines agreement with the FDA on the statistical design and power of the Phase 3 trial, as well as the primary endpoint definition. The SPA states that the trial is adequately designed to provide the necessary data that, depending on the outcome, could support a Biologics License Application (BLA) submission. The SPA does note the general point for all SPAs, that BLA acceptance and approvability are review issues and that a BLA approval will depend on the quality of actual clinical trial data, the robustness of the effect on the stated primary endpoint, the impact on the secondary endpoints, a favorable assessment of the study conduct, and analysis of safety information and other supportive data. We have approximately 50 active clinical sites for this clinical trial and have completed enrollment in September 2021 with 711 patients. The primary endpoint for the clinical trial is DFS. This trial has been designed to have 90% power, a hazard ratio of 0.5 and an alpha of 0.05. We are assuming a 15% improvement in the active arm (CAN-2409) as compared to placebo in the rate of events measured according to the DFS definition provided above. We expect topline data from this Phase 3 trial at the end of 2024.

*Phase 2 Clinical Trial for Active Surveillance*

Clinical results to date suggest that CAN-2409 as monotherapy may reduce the rates of biochemical failure for patients with localized prostate cancer. In the AS setting, we will assess whether CAN-2409 has the potential to delay or prevent tumor progression to a later stage that demands radical treatment.

In May 2019, the Company completed enrollment of 187 patients in its Phase 2 clinical trial of CAN-2409 in patients with low-to-intermediate-risk, localized, non-metastatic prostate cancer, randomized 2:1. The primary endpoint is biopsy-proven progression-free survival (PFS). Progression is defined as an increase in Gleason grade or increase in tumor volume to > 33%. As the primary endpoint is event-driven, in February 2023, based on a blinded review of the event rate, the Company determined that additional time is required for patient follow up in order to collect a sufficient number of events. Based on the current rate of events, the Company currently anticipates topline data to be available in the fourth quarter of 2024.

**CAN-2409 for Non-Small Cell Lung Cancer (NSCLC)**

To assess the potential for CAN-2409 to trigger local and systemic immune activation and produce a “hot” tumor phenotype, we designed and completed a clinical trial in patients with surgically resectable lung cancer. In this proof of mechanism Phase 1 clinical trial, dose escalation of intratumoral neoadjuvant CAN-2409 was followed by tumor resection three weeks later. The specific goal was to obtain biological data to better understand the impact of CAN-2409 on the tumor microenvironment, with a specific focus on intratumoral CD8+ T cell activation and function while assessing effects on the systemic immune response. The effects of CAN-2409 were evaluated by comparing post-injection specimens to an internal control consisting of each patient’s own pre-treatment needle biopsy and blood samples, and an external cohort of matched patients who underwent standard surgical resection without CAN-2409. The results showed evidence of significant intratumoral and systemic immune activation after experimental CAN-2409 monotherapy treatment. Analysis of peripheral blood mononuclear cells, both before and after CAN-2409 administration, demonstrated a significant increase in expression of proliferation and activation markers including HLA-DR, CD38 and Ki67 three weeks after CAN-2409 initiation. Other relevant findings in this clinical trial included an increase in markers of T cell activation such as PD-1 and CTLA-4, which are targets of ICI that have been approved for use in NSCLC.

In this NSCLC Phase 1 clinical trial, two patients experienced grade 3 dehydration with renal insufficiency, two patients presented grade 3 urinary retention and six patients were observed to have a grade 4 low lymphocyte count. Of significant interest, one patient, a 70 year-old male with a 14.8cm stage IIIA sarcomatoid carcinoma, exhibited a nearly 50% decrease in tumor volume at 3 weeks after CAN-2409 monotherapy treatment. Collectively, these results lead us to believe that CAN-2409 could provide an opportunity to improve ICI response rates in patients with NSCLC by eliciting additional immune activation in lung cancer patients.

*CAN-2409 and Checkpoint Combination Phase 2 Clinical Trial for NSCLC in Patients with Inadequate Response to ICI*

In 2020, we initiated a Phase 2 clinical trial in NSCLC patients with inadequate response to ICI that will enroll patients receiving standard of care ICI (plus chemotherapy if indicated) in combination with two courses of CAN-2409 plus continued ICI. This open label clinical trial, as amended, is targeting enrollment of approximately 80 patients with stage III/IV NSCLC in two separate cohorts. The cohorts are defined based on response to ICIs at the time of enrollment. Cohort 1 addresses patients with stable disease and Cohort 2 enrolls patients with progressive disease after at least 18

weeks of ICI treatment. Patients will continue treatment with their initial ICI and CAN-2409 will be added to their regimen. The primary efficacy endpoint for this trial is response rate measured by RECIST and/or Disease Control Rate.

We reported initial data from this trial at the ASCO Annual Meeting in June 2022. During our Research and Development Day in December 2022, we presented updated data demonstrating evidence of local and systemic anti-tumor activity; a disease control rate of 77% (20/26) in patients entering trial with disease progression (cohort 2); sustained and ongoing clinical responses greater than 1 year; favorable change in the trajectory of tumor progression; decreased tumor size of RECIST target lesions in most patients; reduced uninjected tumor size in 14/21 patients (67%); an overall response rate of 13% (4/30) across cohorts 1 and 2; durable disease stabilization translating into encouraging preliminary evidence of progression-free survival; consistent induction of local and systemic cytotoxic T cell response; increased infiltration of CD8+ T cells in the tumor microenvironment; systemic expansion of effector T cells and increase in soluble granzyme B levels in the peripheral blood; and favorable safety/tolerability data with most treatment-related adverse events being grade 1/2.

We anticipate presenting additional updated data from this ongoing Phase 2 clinical trial in the third quarter of 2023.

**CAN-2409 for Pancreatic Cancer**

We are currently conducting a randomized Phase 2 clinical trial for CAN-2409 in borderline resectable pancreatic cancer, with a target enrollment of up to 54 patients. In March 2023, in connection with our cost management and dynamic portfolio management initiatives, we elected to pause new enrollment in this randomized Phase 2 clinical trial, subject to additional funding. Despite the pause in patient enrollment, we continue to expect to present initial clinical data in the fourth quarter of 2023. In a previous Phase 1b clinical trial, patients with pancreatic cancer treated with CAN-2409 in addition to standard of care demonstrated a greater survival duration over the expected survival of the patients treated with the existing standard of care alone in a comparison to historical trial results. Furthermore, in the subset of patients where pre- and post-treatment tumor biopsies were available, a statistically significant increase in the number of CD8+ tumor infiltrating lymphocytes was observed. In addition, the study demonstrated that CAN-2409 was generally well-tolerated in combination with standard of care.

**CAN-2409 for High-Grade Glioma**

*Phase 3 Clinical Trial of CAN-2409 in High-Grade Glioma*

At our Research & Development Day in December 2022 we announced that we have made a portfolio and resource prioritization decision to pursue CAN-3110 in recurrent HGG, but not to pursue a Phase 3 clinical trial of CAN-2409 in high-grade glioma. The CAN-3110 program in recurrent HGG may serve as an enabling clinical trial for future expansion into earlier stages of HGG as well as other solid tumors outside the brain that are characterized by Nestin expression.

*Phase 1 Clinical Trial of CAN-2409 With Opdivo in High-Grade Glioma*

We conducted a Phase 1 clinical trial in patients with newly diagnosed HGG examining the combination of CAN-2409 and anti-PD-1 nivolumab (Opdivo, BMS) in collaboration with BMS and Adult Brain Tumor Consortium. This was the first clinical trial to evaluate the combination of CAN-2409 and nivolumab in HGG patients with the goal of enhancing anti-tumor T cell activation and expansion and the potential for better clinical outcome.

Data for this Phase 1 clinical trial were presented at the 37th Annual Meeting of Society for Immunotherapy of Cancer (SITC) in Boston in November 2022. In the trial involving 35 evaluable patients, extensive biomarker analyses demonstrated that the combination of CAN-2409 and nivolumab resulted in a statistically significant expansion of activated tumor-fighting CD4+ and CD8+ T cells effector cells as well as decreased markers of exhaustion on effector cells. Proteomic analysis by OLINK revealed an increase in pro-inflammatory cytokines, including interferon-gamma, the chemokines CXCL9/10 and CXCL11, MCP-1, MCP-3, and granzyme A. Systemic immune activation was observed after the single administration of CAN-2409, prior to initiation of nivolumab (week 3 post treatment). Median overall survival (mOS) for patients with methylated MGMT promoter was 30.6 months for those who underwent gross total resection (GTR) (n=10) and 12.6 months for those who underwent sub-total resection (STR) (n=5). mOS for patients with unmethylated MGMT was 13.2 months (GTR) (n=16) and 15.9 months (STR) (n=4), respectively.

*Phase 1b/2 Clinical Trial of CAN-2409 Combined with Standard of Care in High-Grade Glioma*

In our Phase 1b/2 clinical trial in newly diagnosed patients with HGGs, including the difficult-to-treat glioblastoma, CAN-2409 demonstrated a statistically significant increase in patient survival when combined with current standard of care over the current standard of care alone (surgery, radiation and temozolomide). The trial compared the overall survival of 48 enrolled patients treated at 4 clinical sites with CAN-2409 plus standard of care against a matched controlled set of 134 patients enrolled at MGB who received only standard of care. The results demonstrated that the median overall survival of patients receiving standard of care alone was 13.5 months while patients receiving CAN-2409 plus standard of care was 17.1 months (p=0.0417). Importantly, a pre-planned analysis on a subset of patients treated surgically with gross total resection (>95% of tumor removed) during surgery (18 patients compared to 44 in the control arm),

demonstrated a median overall survival of 25.1 months in the CAN-2409 arm versus 16.3 months in the standard of care group, with approximately a 50% improvement (p=0.0120). In this patient population, after three years, one in three patients was alive in the CAN-2409 arm compared to 1 in 20 patients in the standard of care group. At the end of the study, three of the patients who received CAN-2409 were alive without progression after 43, 62.1 and 88.5 months. CAN-2409 was generally well tolerated, with most treatment-related adverse events being grade 1 or 2, and few reports of grade 3 or 4 events.

**Opportunities for CAN-2409 in Other Cancer Indications**

In addition to patients with prostate, lung, pancreatic, and brain cancer, CAN-2409 has been dosed in small early-stage exploratory clinical trials in patients with ovarian cancer, malignant pleural effusion, pediatric brain cancer and retinoblastoma, supporting the tolerability and safety profile described above.

**CAN-3110 for Recurrent High-grade Glioma**

Our first HSV-based product candidate, CAN-3110, is in an ongoing investigator-sponsored Phase 1 clinical trial in recurrent HGG. This is an open-label, single center, dose-escalation clinical trial in patients who have failed standard of care. The primary endpoint of this clinical trial is to analyze the safety of CAN-3110 use in patients with recurrent HGG. No dose-limiting toxicities were observed in doses ranging from $1x10^6$ to $1x10^{10}$ PFU in half-log increments. 51 patients have been treated.

Immunohistology studies showed persistent presence of HSV antigen and infiltration by CD8+ cytotoxic tumor infiltrating lymphocytes post treatment, providing support for the expected mechanism of action of CAN-3110.

We are particularly encouraged by the clinical course of a few patients who received a single injection with CAN-3110 as monotherapy upon recurrence of glioblastoma. One patient, originally diagnosed with multicentric glioblastoma and initially treated with standard of care surgical resection followed by temozolomide and radiotherapy has been treated with CAN-3110 monotherapy, upon recurrency with development of two lesions visualized on MRI. One lesion, in the frontal region, had developed at the site of the initially resected mass. The second, larger mass was a new lesion. The patient received CAN-3110 via stereotactic administration into the injected lesion. At day 56 post-injection, there was a visible decrease in the volume of both masses. By day 112 post-injection, the volume of both masses was further reduced and the patient was able to go back to work. The patient eventually developed a third lesion, experienced a stroke secondary to a diagnostic procedure, and refused further treatment, dying approximately 15 months after entering the trial. A second patient initially diagnosed with methylated grade IV HGG located in the temporal lobe underwent 2 consecutive resections and treatment with chemoradiation for rapid progressive disease. The patient was injected with CAN-3110 (10E8 pfus), at the site of the original lesion. An MRI scan performed at day 91 showed increased enhancement at the site of injection. The patient underwent an additional resection, but, importantly, histological report showed mainly inflammatory tissue with high density of tumor infiltrating lymphocytes. The patient did not have detectable disease, in absence of any additional treatment for more than 2 years and passed away as passenger of a motor vehicle accident on day 717 post CAN-3110 treatment. Another patient, originally diagnosed with grade IV astrocytoma, was treated with CAN-3110 for a recurrence following first-line therapy with subtotal resection, chemoradiation and adjuvant temozolomide. At time of recurrence, a mass was evident in the left frontal lobe. The patient was enrolled in arm B of the Phase 1 clinical trial which includes treatment with Cytoxan (24 mg/kg one dose day -2) prior to CAN-3110 injection. Post-treatment scan demonstrated progressive reduction in enhancement with cavitary necrosis at the site of injection. The patient remains clinically stable as of February 2023 and has not required additional therapies up to day 350 post CAN-3110. We find these case reports to be encouraging because of the unusually favorable disease course experienced by these patients with recurrent HGG who had previously failed standard of care treatment, in absence of concurrent therapies. Additionally, we have observed a median overall survival of 11.6 months in the Phase 1 trial in the first 41 patients as of the cutoff date of October 2022. Given the median overall survival of 6-9 months in historical clinical trials of other investigational agents in patients with recurrent HGG, who have failed standard of care treatment we believe this is encouraging evidence of clinical activity. We will continue to assess CAN-3110 in this clinical trial.

**Collaborations and Other Transactions**

We are a party to various license and collaboration agreements under which we license patents, patent applications and other intellectual property to and from third parties. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license and collaboration agreements to be material to our business:

***Periphagen.*** On December 9, 2019, we entered into a series of agreements, including an exclusive license agreement, a novation agreement, an equipment purchase agreement and an intellectual property assignment agreement, collectively the Periphagen Agreements, with Periphagen, whereby we acquired certain assets and licensed certain rights (including specified patent rights and know-how, or the Licensed IP Rights) of Periphagen, primarily consisting of exclusive rights to their technology platform and a portfolio of pre-clinical, development stage virus vectors, as well as certain physical property and equipment. The primary classes of assets are HSV-derived assets expressing

neurotrophin-3 (or NT-3 Assets) and other HSV-derived assets (Gene Transfer Neuro-Assets). Under the license agreement, Periphagen granted us a worldwide exclusive license with the right to grant sublicenses through multiple tiers under the Licensed IP Rights to conduct research and to develop, make, have made, use, have used, offer for sale, have sold, export and import products incorporating the Licensed IP Rights in all fields of use except the treatment, diagnosis, and prevention of nononcologic skin diseases and conditions (including use as an aesthetic).

In addition, pursuant to the Periphagen Agreements, we undertook certain commitments and obligations, including the assumption of Periphagen's outstanding loan in the principal amount of $1,000,000 with Diamyd Medical, AB. The promissory note has a contractual interest rate of 2% compounded annually, with the outstanding balance and accrued interest due upon maturity in November 2027, with no interim installments.

In consideration for the licenses under the Periphagen Agreements, we paid Periphagen $811,000 upon signing and agreed to make the following royalty and other payments:

- NT-3 Assets: a single digit percentage of net sales of NT-3 Assets, or, if applicable, a percentage of royalties received by us in the event of a license, sublicense, assignment or other transfer to a third party for commercialization (but no greater than the original royalty percentage we would be required to pay in the event we did not license, sublicense, assign or transfer NT-3 Assets);
- Gene Transfer Neuro-Assets: a single digit percentage of net sales of Gene Transfer Neuro-Assets, or, if applicable, a percentage of royalties received by us in the event of a license, sublicense, assignment or other transfer to a third party for commercialization to treat certain conditions and diseases (but no greater than the original royalty percentage we would be required to pay in the event we did not license, sublicense, assign or transfer Gene Transfer Neuro-Assets);
- Combination Products: a certain percentage (based on the weighted average sale price of NT-3 Assets, or Gene Transfer Neuro-Assets, as applicable) of net sales of combination products; and
- Disposition Income: (i) a single digit royalty rate of certain consideration we receive for the grant of a license, assignment or other intellectual property rights related to the NT-3 Assets and (ii) if we consummate a strategic collaboration with certain specified parties to treat non-oncolygic neurological conditions and diseases, either 2nd decile (if consummated within 18 months) or mid-2nd decile to mid-3rd decile (if consummated thereafter) royalty rates of certain consideration we receive for the grant of a license, assignment or other intellectual property rights related to the Gene Transfer Neuro-Assets.

If we are required to pay royalties to a third party on any product covered under the Periphagen Agreements, we may credit such royalty payments against the royalties owed to Periphagen in the applicable country, up to a percentage reduction in the mid-2nd decile.

The exclusive license agreement with Periphagen (the Periphagen License Agreement) requires us to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset, which includes certain specified clinical milestones. If we fail to use such efforts, subject to dispute and escalation provisions in the Periphagen License Agreement, then we may submit a specified payment in lieu of satisfying such obligations. If we fail to do so, Periphagen may terminate the Periphagen License Agreement for material breach. On December 15, 2022, Periphagen provided notice purporting to terminate the Periphagen License Agreement claiming we failed to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset. We have denied Periphagen's claim and the parties are engaged in the dispute and escalation provisions under the Periphagen License Agreement. See Part I, Item 3 "Legal Proceedings".

The Periphagen License Agreement expires on the later of December 9, 2069 or the end of the Royalty Term. Upon expiration, we will have a fully paid-up, non-exclusive license to make, use, sell, offer for sale and import any products that incorporate the Licensed IP Rights. The Royalty Term means, on a product-by-product and country-by-country basis, the period starting on the first commercial sale of such product in such country and concluding on the later of (i) expiration of patent coverage under the Licensed IP Rights or regulatory exclusivity for such product in such country; or (ii) the date that a certain amount of generic competition exists in such country, provided that no Royalty Term shall exceed 30 years.

The Periphagen License Agreement may be terminated (i) by us for convenience upon 90 days' prior written notice to Periphagen, (ii) by Periphagen if we remain in breach of the Periphagen Agreement following a cure period to remedy the breach or (iii) by Periphagen if we become bankrupt, file for bankruptcy or otherwise become insolvent or are placed in receivership.

***Mass General Brigham (MGB).*** On January 20, 2018, we entered into an exclusive option agreement (the Option Agreement) with MGB. Pursuant to the Option Agreement, we obtained the exclusive right from MGB to negotiate an exclusive worldwide, royalty-bearing license to develop and commercialize products covered by certain MGB patents, including those patents covering CAN-3110, in the field of gene therapy and vector therapy for the treatment or

prevention of cancerous tumors in humans or animals, as such field is further detailed in the Option Agreement (Licensed Field). In consideration for MGB's granting of the exclusive option, we paid MGB a non-refundable fee of $40,000.

Under the Option Agreement, we were required to use reasonable efforts to enter into a clinical trial agreement with MGB. We entered into such clinical trial agreement with MGB (MGB Clinical Trial Agreement) on June 19, 2018. Under the MGB Clinical Trial Agreement, we have committed to remitting up to $750,000 for the performance of a specified Phase 1 clinical trial by MGB pursuant to a protocol summary contained in the Option Agreement.

On September 15, 2020, we exercised our option and entered into an exclusive patent license agreement with MGB (the MGB License Agreement). Under the MGB License Agreement, MGB granted to us (a) an exclusive, royalty-bearing license under certain of MGB's patents to make, have made, use, have used, sell and have sold certain products covered by such licensed patents (the Licensed Products) and otherwise practice processes covered by such licensed patents (Licensed Processes); and (b) a non-exclusive, royalty-bearing license under certain other of MGB's patents to make, have made, use, have used, sell and have sold Licensed Products, but not to sell or have sold Licensed Processes. The foregoing rights are sublicensable, subject to sublicensing terms set forth in the MGB License Agreement. In connection with executing the MGB License Agreement, we paid a license issue fee of $100,000. We also agreed to reimburse MGB for all reasonable fees and expenses MGB had incurred and will incur for the preparation, filing, prosecution and maintenance of the licensed patent rights, in an amount equal to $141,268.

Under the MGB License Agreement, we are required to use commercially reasonable efforts to develop and make available to the public Licensed Products in the Licensed Field, which efforts include certain milestones detailed in the MGB License Agreement.

Under the MGB License Agreement, prior to the first commercial sale of the Licensed Products, we are required to pay MGB an annual license fee beginning on the fourth anniversary of the effective date. Following the first commercial sale of the Licensed Products, we are required to pay MGB an annual minimum royalty, which amount may be credited against earned royalties starting in the fourth year following the first commercial sale.

In addition to such annual license fee and royalty obligations, the MGB License Agreement contains cumulative milestone payments for up to a maximum amount of $39,000,000, upon the achievement of various clinical, commercial and sales milestones of clinical and commercial development and sales, certain of which milestones apply to development and sale of any Licensed Product as a monotherapy and certain of which milestones apply to development and sale of any Licensed Product in combination with another therapy modality for the treatment of solid tumors.

We are required to pay royalties to MGB upon first commercial sale of the Licensed Products, which are paid at an increasing rate as net sales increase, ranging from low single digits to high single digits. We also agreed to pay a single digit royalty rate on net sales of any products developed using certain MGB know-how but which is not covered by the licensed patent rights, or derived products.

We may reduce our royalty obligations to MGB on any product (but not derived products) by an agreed-upon percentage if we are required to pay a royalty to a third party to avoid patent infringement claims in respect of our development and commercialization of Licensed Products. The royalty rate paid to MGB may not fall below a pre-specified percentage for the sale of any product and another percentage for the sale of any derived product.

Our obligation to pay royalties to MGB expires on a country-by-country basis on the latest of (i) the date upon which there ceases to be a valid claim of patent rights as further detailed in the MGB License Agreement in such country, (ii) expiration of statutory or regulatory exclusivity in such country and (iii) 10 years after the first commercial sale.

The MGB License Agreement also requires us to pay a percentage of any non-royalty income attributable to the sublicense, including (i) 2nd decile rates if such sublicense occurs prior to dosing the first patient in a Phase 2 trial, (ii) 1st decile rates if such sublicense occurs after dosing the first patient in a Phase 2 trial but before approval of a BLA by the FDA (or the equivalent approval and regulatory body in another major market country) and (iii) single digit rates if such sublicense occurs after approval of a BLA by the FDA (or the equivalent approval and regulatory body in another major market country).

The MGB License Agreement expires on the latest of (i) the 10th anniversary of the first commercial sale in the last country which has a commercial sale, (ii) the date on which all relevant issued patents and filed patent applications have expired or been abandoned and (iii) upon the expiration of market exclusivity on the applicable product.

The MGB License Agreement may be terminated by MGB (i) if we fail to pay any amounts owed under the terms of the agreement within a specified cure period, (ii) if we fail to maintain insurance in accordance with the MGB License Agreement, (iii) if we file for bankruptcy, or (iv) if we remain in default of the MGB License Agreement for non-financial reasons following a specified cure period to remedy the breach. The MGB License Agreement may be terminated by us for convenience upon 90 days' prior written notice.

***Ventagen.*** On March 1, 2014, we entered into an exclusive license agreement (the Ventagen Agreement), with Ventagen, LLC (Ventagen). The Ventagen Agreement provides Ventagen an exclusive license, with rights to grant sublicenses (subject to certain terms and conditions) under any worldwide patent rights and know-how owned or controlled by us during the term of the Ventagen Agreement which cover applicable technology utilizing the delivery method of the herpes derived TK protein to tumors or other tissues via a viral vector (as further specified therein), to research, use, have used, import, have imported, export, have exported, offer for sale, have sold, sell, distribute and market certain products for the prevention or treatment of cancer in humans and any use in animals (or the Field of Use) (Licensed Products), for commercial sale and distribution within Mexico, Belize, Guatemala, Honduras, El Salvador, Costa Rica, Nicaragua, Panama, Colombia and Bolivia (or the Territory).

Under the Ventagen Agreement, Ventagen agreed to use commercially reasonable efforts to develop and commercialize Licensed Products in the Territory in the Field of Use.

Ventagen agreed to pay us $1,000,000 for research and development, which we received in 2014 and 2015, and agreed to pay us a fixed future milestone payment of $2,500,000 upon Ventagen's achievement of a specified amount of sales of a Licensed Product, which is subject to certain reductions for our direct cost over a specified threshold.

Ventagen also agreed to purchase all of its clinical and commercial supply of Licensed Products from us required for clinical or commercial purposes at a price of cost plus a specified increase of the wholesale price of the Licensed Products, subject to a minimum and maximum price, through the end of the Royalty Term, which is defined as the period commencing on the effective date of the Ventagen Agreement and ending on a country-by-country basis on the later of (i) the last expiration date of the patent rights covering a Licensed Product, (ii) twelve years from the receipt of marketing authorization of the Licensed Product in the applicable country, or (iii) the date a generic version of a Licensed Product that is manufactured, owned or controlled by a third party is granted a market authorization. If we are unable or unwilling to manufacture supply under the terms of the Ventagen Agreement, Ventagen has the right to manufacture its own supply and will be required to pay to us a fixed fee per dose sold by Ventagen, its affiliates, agents, sublicensee or end users. We have also agreed to provide certain services to Ventagen related to Ventagen's development plan.

The Ventagen Agreement expires on the date of the expiration of the final Royalty Term in all countries in the Territory. The Ventagen Agreement may be terminated (i) by Ventagen at will upon 30 days' prior written notice to us, (ii) by us subject to a specified notice period if Ventagen files for bankruptcy or becomes insolvent or (iii) by us if Ventagen remains in material breach of the Ventagen Agreement following notice and a cure period to remedy the breach. Ventagen retains an irrevocable, perpetual, paid up, royalty-free license, with rights of sublicense to use, have used, lease, import and export, offer to sell, sell, have sold, product, distribute and market Licensed Products in each country in the Territory after the expiration of the Royalty Term in such country.

Certain of our current stockholders own 49.5% of the voting stock of Ventagen, but we do not hold any management position or run the day-to-day operations of Ventagen. See "Certain Relationships and Related Person Transactions."

**Competition**

The development and commercialization of new product candidates is highly competitive. We face competition from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others with respect to CAN-2409 and CAN-3110 and will face similar competition with respect to any product candidates that we may seek to develop or commercialize in the future. We compete in pharmaceutical, biotechnology and other related markets that develop immuno-oncology therapies for the treatment of cancer. There are other companies working to develop viral immunotherapies for the treatment of cancer including divisions of large pharmaceutical and biotechnology companies of various sizes. The large pharmaceutical and biotechnology companies that have commercialized and/or are developing immuno-oncology treatments for cancer include AstraZeneca, Bristol-Myers Squibb, Gilead Sciences, Merck & Co., Novartis, Pfizer and Genentech.

Some of the products and therapies developed by our competitors are based on scientific approaches that are the same as or similar to our approach, including with respect to the use of viral immunotherapy with adenovirus and HSV. Other competitive products and therapies are based on entirely different approaches. We are aware that Oncorus, Inc., Replimune Group, Inc., Amgen Inc., Astellas Pharma, Inc, Istari Oncology Inc, Orca Therapeutics, B.V., CG Oncology, Inc, ImmVira Co., Ltd., IconOVir Bio, Inc., and FerGene, Inc., among others, are developing viral immunotherapies that may have utility for the treatment of indications that we are targeting. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of the companies we compete against or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in the concentration of even more resources among a smaller

number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, in establishing clinical trial sites and enrolling subjects for our clinical trials and in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination of our commercial opportunity if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, or are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or foreign 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 we are able to enter the market. The key competitive factors affecting the success of all our product candidates, if approved, are likely to be their efficacy, safety, convenience and price, if required, the level of biosimilar or generic competition and the availability of reimbursement from government and other third-party payors.

**Commercialization**

We intend to retain significant development and commercial rights to our product candidates and, if marketing approval is obtained, to commercialize our product candidates on our own, or potentially with a partner, in the United States and other regions. We currently have no sales, marketing or commercial product distribution capabilities and have no experience as a company commercializing products. We intend to build the necessary infrastructure and capabilities over time for the United States, and potentially other regions, following further advancement of our product candidates. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure and manufacturing needs may all influence or alter our commercialization plans.

**Manufacturing**

We have established an operations leadership team with extensive experience in manufacturing biologics based on viruses, including viral immunotherapy products and gene therapy products, and in the construction, validation, approval and operation of facilities designed to manufacture biologics. We have secured a third-party contract manufacturing organization for clinical and commercial-scale manufacturing of our CAN-2409 product candidates. We are also currently evaluating various options for the clinical-scale manufacture of our CAN-3110 product candidate, including the development of clinical-scale manufacturing capabilities at our own facility.

**Intellectual Property**

We believe that approval of our CAN-2409 and CAN-3110 product candidates under a BLA may result in 12 years of data exclusivity in the United States under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the ACA), 10 years of market exclusivity in Europe and significant durations in other markets, which would be complementary to any relevant patent exclusivity.

With regard to patent exclusivities, we have rights to issued composition of matter patents in the United States, Australia, Canada, China, Europe, and Japan and patent applications pending in Australia, Europe, and Korea that relate to CAN-3110. The issued patents and the pending applications, if issued, are expected to expire in 2036. This patent family is exclusively licensed to us. We also own a United States patent and a pending patent application that relate to a method of use of CAN-2409 in combination with a checkpoint inhibitor. The issued patent and the pending application, if issued, are expected to expire in 2034. We also have in-licensed from Periphagen patents and patent applications relating to our enLIGHTEN™ Discovery Platform. These patents and applications, if issued, are expected to expire between 2037 and 2042.

**Government Regulation**

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and licensure under the Public Health Service Act (PHS Act), and other federal, state, local and foreign statutes and regulations. The FD&C Act and corresponding regulations govern, among other things, the research, development, clinical trial, testing, manufacturing, quality control, approval, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, marketing, promotion, export and import, advertising, post-approval monitoring, and post-approval reporting involving biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Further, even if we obtain the required regulatory approvals for our products, pharmaceutical companies are subject to myriad federal, state, and foreign healthcare laws, rules, and regulations governing all aspects of our operations, including, but not limited to, our relationships with healthcare professionals, healthcare institutions, distributors of our products, and sales and marketing personnel; governmental and other third-party payor coverage and reimbursement of our products; and data privacy and security. Such laws, rules, and regulations are complex, continuously evolving, and, in many cases, have not been subject to extensive interpretation by applicable regulatory agencies or the courts. We

are required to invest significant time and financial resources in policies, procedures, processes, and systems to ensure compliance with these laws, rules, and regulations, and our failure to do so may result in the imposition of substantial monetary or other penalties by federal or state regulatory agencies, give rise to reputational harm, or otherwise have a material adverse effect on our results of operations and financial condition.

**United States Biological Products Development Process**

The process required by the FDA before a biological product candidate may be licensed for marketing in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies performed in accordance with FDA's good laboratory practices (GLPs) requirements and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an investigational new drug application (IND) which must become effective before human clinical trials may begin;
- approval of the protocol and related documentation by an IRB or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to good clinical practices (GCPs) requirements and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product candidate for its intended use;
- preparation of and submission to the FDA of a BLA for marketing approval that includes sufficient evidence of establishing the safety, purity, and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to accept and file the application;
- satisfactory completion of an FDA pre-license inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practices (cGMPs) to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- satisfactory completion of an FDA advisory committee review, if applicable;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA in accordance with any applicable expedited programs or designations;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies); and
- FDA review and approval, or licensure, of the BLA to permit commercial marketing of the product for specific indications for use in the United States.

**Pre-clinical Studies and the IND Process**

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

Prior to commencing an initial clinical trial in humans with a product candidate in the United States, an IND must be submitted to the FDA and the FDA must allow the IND to proceed. An IND is an exemption from the FD&C Act that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA allowance that such investigational product may be administered to humans in connection with such trial. Such authorization must be secured prior to interstate shipment and administration. In support of a request for an IND, the clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND must become effective before human clinical trials may begin. Once submitted, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the IND on a full or partial clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial or part of the study can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. The FDA also may impose clinical holds on a sponsor's IND at any time before or during clinical trials due to, among other considerations, unreasonable or significant safety concerns, inability to assess safety concerns, lack of qualified investigators, a misleading or materially incomplete investigator brochure,

study design deficiencies, interference with the conduct or completion of a study designed to be adequate and well-controlled for the same or another investigational product, insufficient quantities of investigational product, lack of effectiveness, or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA.

**Clinical Trials**

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under control of the trial sponsor. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters and criteria to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to trial subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee (DSMB). This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the trial and may recommend halting the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

Certain information about certain clinical trials must also be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

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

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the biological product candidate in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2. The biological product candidate is evaluated in a limited patient population with a specific disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. The biological product candidate is administered to an expanded patient population to further evaluate dosage, clinical efficacy, potency, and safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for approval and product labeling.

In March 2022, the FDA released a final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology biological product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to biological product development and reduce developmental costs and time.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may also be made a condition to approval of the BLA. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the biological product as well as finalize a process for

manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the Public Health Service Act (PHS Act), emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

Both the FDA and the EMA provide expedited pathways for the development of biological product candidates for treatment of rare diseases, particularly life threatening diseases with high unmet medical need. Such biological product candidates may be eligible to proceed to registration following a single clinical trial in a limited patient population, sometimes referred to as a Phase 1/2 trial, but which may be deemed a pivotal or registrational trial following review of the trial's design and primary endpoints by the applicable regulatory agencies. Determination of the requirements to be deemed a pivotal or registrational trial is subject to the applicable regulatory authority's scientific judgement and these requirements may differ in the United States and the European Union.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

**U.S. Review and Approval Processes**

Assuming successful the completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include results of product development, laboratory and animal studies, human clinical trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review to determine if it is substantially complete before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial application user fee, although the fee may be waived under certain circumstances. Under the performance goals and policies implemented by the FDA under the Prescription Drug User Fee Act (PDUFA) for original BLAs, the FDA targets ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. This review typically takes twelve months from the date the BLA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure and potent for its intended use and whether the product is being manufactured in accordance with cGMP to ensure its continued safety, purity and purity. The FDA may refer applications for novel biological products or biological products that present difficult or novel questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for

review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy (REMS) is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Under the Pediatric Research Equity Act (PREA) a BLA or supplement to a BLA for a novel product (e.g., new active ingredient, new indication, etc.) must contain data to assess the safety and effectiveness of the biological 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. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, including to subpopulations of patients, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, precautions or interactions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing trials. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

**Orphan Product Designation**

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

Orphan product designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. If a product that has orphan product designation subsequently receives the first FDA approval for a particular active ingredient for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan product exclusivity. Competitors,

however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if a product candidate is determined to be contained within the competitor's product for the same indication or disease. If a biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug status in the European Union (EU) has similar, but not identical, benefits.

**Expedited Development and Review Programs**

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions. To be eligible for fast track designation, new drugs and biological product candidates must be intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during the clinical development of the product. One benefit of fast track designation, for example, is that the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review.

Under the FDA's breakthrough therapy program, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation comes with all of the benefits of fast track designation. The FDA may take other actions appropriate to expedite the development and review of the product candidate, including holding meetings with the sponsor and providing timely advice to, and interactive communication with, the sponsor regarding the development program.

A product candidate is eligible for priority review if it treats a serious or life-threatening disease or condition and, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Under priority review, the FDA's goal is to review an application in six months once it is filed, compared to ten months for a standard review. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Additionally, a product candidate may be eligible for accelerated approval. Drug or biological 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, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on an intermediate clinical endpoint other than survival or irreversible morbidity or mortality, that is reasonably likely to predict irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials, which must be conducted with due diligence, to verify the clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit and, under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date accelerated approval was granted. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials, intended for dissemination or publication be submitted to the agency for review. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

**Post-Approval Requirements**

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements, as well as requirements relating to record keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. Manufacturers of products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, 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 release by the FDA, the manufacturer submits samples of each lot of product to the FDA 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. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

Manufacturers must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, product detentions or refusal to permit the import or export of the product, restrictions on the marketing or manufacturing of the product, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors or other stakeholders, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products 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 cGMPs, which impose certain procedural and documentation requirements on sponsors and their contract manufacturing organizations (CMOs). Manufacturers and other parties involved in the drug supply chain for prescription drug and biological products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

**U.S. Patent Term Restoration and Marketing Exclusivity**

Depending upon the timing, duration and specifics of the FDA approval of a biological product, some of a sponsor's U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. In addition, a patent can only be extended once and only for a single product. The United States Patent and trademark Office (USPTO) in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our patents, if and as applicable, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

A biological product can obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including some regulatory exclusivity periods tied to patent terms. This six-month

exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA) which created an abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHS Act attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, 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. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

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, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until 12 years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation and impact of the BPCIA is subject to significant uncertainty.

**United States Regulation of Companion Diagnostics**

Our product candidates may require use of an in vitro diagnostic to identify appropriate patient populations. These diagnostics, often referred to as companion diagnostics, are regulated as medical devices. In the United States, the FD&C Act and its implementing regulations and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical 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, companion diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (PMA approval).

If use of companion diagnostic is essential to safe and effective use of a drug or biological product, then the FDA generally will require approval or clearance of the diagnostic contemporaneously with the approval of the therapeutic product. On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel candidates such as our product candidates, a companion diagnostic device and its corresponding drug or biological candidate should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The 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 (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 drug 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 July 2016, the FDA issued a draft guidance document intended to further assist sponsors of therapeutic products and sponsors of in vitro companion diagnostic devices on issues related to co-development of these products.

The FDA generally requires companion diagnostics intended to select the patients who will respond to cancer treatment to obtain approval of a PMA for that diagnostic contemporaneously with approval of the therapeutic. The review of these in vitro companion diagnostics in conjunction with the review of therapeutic candidates such as those we are developing

involves coordination of review by the FDA's Center for Biologics Evaluation and Research and by the FDA's Center for Devices and Radiological Health. 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 applicant 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 also subject to an application fee.

PMAs for certain devices must generally include the results from extensive pre-clinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. In addition, as part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR) which imposes elaborate testing, control, documentation and other quality assurance requirements.

If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or a not-approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will issue an order denying approval of the PMA or issue a not approvable order. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing. PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

**Additional Regulation**

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines.

**Government Regulation Outside of The United States**

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, research and development, clinical trials, testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products as well as authorization and approval of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

**Clinical Trials Regulation**

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, an application must be submitted for each clinical trial to each country's national competent authority (NCA), and at least one independent ethics committee, much like the FDA and an IRB, respectively. Under the new Clinical Trials Regulation (EU) No. 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022, a single application is now made through the Clinical Trials Information System (CTIS) for clinical trial authorization in up to 30 EU/EEA countries at the same time and with a single set of documentation.

The assessment of applications for clinical trials is divided into two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State, however overall related timelines are defined by the Clinical Trials Regulation. The new Clinical Trials Regulation also provides for simplified reporting procedures for clinical trial sponsors.

**European Union Drug Review and Approval**

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization. To obtain regulatory approval of a medicinal product in the EU, we must submit a marketing authorization application (MAA). A centralized marketing authorization is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA, and is valid throughout the EU and the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway) (the EEA). The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicinal products (i.e. gene therapy, somatic cell therapy or tissue-engineered medicines), and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

The application used to submit the BLA in the United States is similar to that required in the European Union, although there may be certain specific requirements, for example those set out in Regulation (EC) No 1394/2007 on advanced therapy medicinal products, covering gene therapy, somatic cell therapy and tissue-engineered medicinal products.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain is no longer covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January, 1 2021. For a period of three years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of marketing authorizations made by the European Medicines Agency and certain other regulators when determining an application for a new Great Britain marketing authorization.

**Data and Market Exclusivity**

In the EU, upon receiving a marketing authorization, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, are held to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

**Orphan Drug Designation and Exclusivity**

Products receiving orphan designation in the EU can receive ten years of market exclusivity, during which time no "similar medicinal product" may be placed on the market. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan medicinal product can also obtain an additional two years of market exclusivity in the EU where an agreed pediatric investigation plan (PIP) for pediatric studies has been complied with. No extension to any supplementary protection certificate (SPC) can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a product may be designated as an orphan medicinal product if it meets the following criteria: (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five (5) in ten thousand (10,000) persons in the EEA when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product would be of significant benefit to those affected by that condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon the grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, a marketing authorization may be granted to a similar medicinal product for the same indication at any time if:

- the second applicant can establish that its product, although similar to the authorized orphan product, is safer, more effective or otherwise clinically superior;
- the marketing authorization holder of the authorized product consents to a second orphan medicinal product application; or
- the marketing authorization holder of the authorized product cannot supply enough orphan medicinal product.

**Pediatric Development**

In the EU, companies developing a new medicinal product must agree upon a PIP with the EMA's pediatric committee (PDCO) and must conduct pediatric clinical trials in accordance with that PIP, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the product for which a marketing authorization is being sought. The MAA for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be

completed at a later date. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under an SPC (provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to 2 years before the SPC expires) even where the trial results are negative. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

**Post-Approval Controls**

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include the following:

- The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs).
- All new MAAs must include a risk management plan (RMP) describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.
- All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics (SmPC) and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

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

The UK formally left the EU on January 31, 2020, and the UK and the EU have concluded a trade and cooperation agreement or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland). Except in respect of the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore largely aligns with current EU medicines regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. However, notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under the new framework mentioned above which will be put in place by the MHRA from January 1, 2024, the MHRA has stated that it will still take into account decisions on the approval of marketing authorizations from the EMA (and certain other regulators) when considering an application for Great Britain marketing authorization.

**Health Reform**

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and continues to significantly impact the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition to coverage under Medicare Part D for the manufacturer's outpatient drugs.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted:

- The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. Subsequent legislation extended the 2% payment reduction which remains in effect through 2030.
- The American Taxpayer Relief Act further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.
- On April 13, 2017, the Centers for Medicare & Medicaid Services (CMS) published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- 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 new drug 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives which could limit the amounts that federal and state governments will pay for healthcare products and services and result in reduced demand for certain pharmaceutical products or additional pricing pressures. The Inflation Reduction Act of 2022, or IRA, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $2,000 starting in 2025; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. presidential executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

President Biden has also issued multiple executive orders that have sought to reduce prescription drug costs. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate

demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

**Coverage and Reimbursement**

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. Thus, even if a product candidate is approved, sales of the product 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, the product. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party 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, reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

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. 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. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.

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, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party 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.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products 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 payor 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 regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European

Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. 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 our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

**Other Healthcare Laws and Compliance Requirements**

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, 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. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

The federal civil and criminal false claims laws, including the civil False Claims Act (FCA) prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.

The federal civil monetary penalties laws impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary, if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies.

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity may be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their respective business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.

The Physician Payments Sunshine Act, enacted as part of the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed health care practitioners and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

**Federal Consumer Protection and Unfair Competition Laws Broadly Regulate Marketplace Activities and Activities That Potentially Harm Consumers.**

Analogous state and foreign laws and regulations, including, but not limited to, state anti-kickback and false claims laws, may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and relevant federal government compliance guidance; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers; restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws may govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do 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 related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement 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 are found to not be in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

**Employees and Human Capital Resources**

As of December 31, 2022, we had 76 employees. Of these employees, 61 perform research and development functions. None of our employees are represented by a labor union and we believe we maintain good relations with our employees.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

**Legal Proceedings**

From time to time, we may become involved in litigation or other legal proceedings. On December 15, 2022, Periphagen notified us by letter of its claim that we have failed to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset under an Exclusive License Agreement dated December 9, 2019 between us and Periphagen (the "Periphagen License Agreement"). We have denied Periphagen's claims. On January 13, 2023, we

filed a demand for arbitration against Periphagen with the American Arbitration Association, seeking a declaration that Periphagen's December 15 letter failed to comply with the dispute and escalation provisions in the Periphagen License Agreement. After filing the demand, the parties began engaging in the dispute and escalation process under the Periphagen License Agreement. On March 10, 2023, Periphagen filed its answer and counterclaims to our demand for arbitration. In its counterclaims, Periphagen seeks a declaration that we have not used commercially reasonable efforts to complete a human proof of concept clinical trial of the NT-3 Asset and a declaration that any further extension of time would not be scientifically or commercially reasonable. Periphagen also seeks a declaration that we must use commercially reasonable efforts to develop the NT-3 Asset during any remaining time under the agreement. We have denied Periphagen's counter claims.

In the event the parties are unable to resolve the dispute as part of the escalation process, an arbitrator will decide whether we have used commercially reasonable efforts. In the event that the arbitrator determines that we have not used commercially reasonable efforts, then we may submit a specified payment in lieu of satisfying such obligations.

Aside from the proceeding with Periphagen, we are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

**Corporate Information**

We were incorporated in Delaware in June 2003. On November 30, 2020, the Company changed its name to Candel Therapeutics, Inc. Our principal executive offices are located at 117 Kendrick Street, Suite 450, Needham, Massachusetts 02494. Our telephone number is (617) 916-5445 and our e-mail address is investors@candeltx.com. Our Internet website address is www.candeltx.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act), are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (SEC). Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through the "Corporate Governance" portion of our website.

**Item 1A. Risk Factors.**

*Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See "Forward-Looking Statements" for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.*

**Risks Related to Our Business, Financial Position and Capital Requirements**

***We are a biopharmaceutical company with a limited operating history and have not generated any revenue to date from product sales.***

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated under the laws of the State of Delaware in June 2003. Since inception, we have focused substantially all of our efforts and financial resources on raising capital and developing our initial product candidates. To date, we have financed our operations primarily through the issuance and sale of our convertible preferred stock to outside investors in private equity financings and from the proceeds of the initial public offering of our common stock (the IPO). From our inception through December 31, 2022, we raised an aggregate of $145.2 million of gross proceeds from such transactions. In addition, in February 2022, we borrowed $20.0 million under the Loan Agreement with SVB. As of December 31, 2022, our cash and cash equivalents were $70.1 million. We have incurred net losses in each year since our inception, and we had an accumulated deficit of $99.2 million as of December 31, 2022. For the years ended December 31, 2022 and 2021, we reported net losses of $18.9 million and $36.1 million, respectively. We have no products approved for commercial sale and therefore have never generated any revenue from product sales, and we do not expect to do so in the foreseeable future. We have not obtained regulatory approvals for any of our product candidates, and even if our clinical development efforts result in positive data, our product candidates may not receive regulatory approval or be successfully introduced and marketed at prices that would permit us to operate profitably.

We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

***We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.***

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our research and development expenses to significantly increase in connection with the commencement and continuation of clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we will incur significant sales, marketing and manufacturing expenses. We are incurring additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

The amount of our future losses is uncertain, and our quarterly and annual operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

- Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:
- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully enroll and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain marketing approval for our product candidates, and the timing and scope of any such approvals we may receive;

- the changing and volatile U.S. and global economic environments, including as a result of the COVID-19 pandemic;
- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production, and the success of achieving clinical-scale manufacturing operations in our new facility and commercial and clinical-scale manufacturing at third-party manufacturers
- our ability to attract, hire and retain qualified personnel;
- expenditures that we will or may incur to develop additional product candidates;
- the level of demand for our product candidates should they receive approval, which may vary significantly;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

***We have no products approved for commercial sale and have not generated any revenue from product sales.***

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our product candidates, and we do not expect to generate any revenue from the sale of products in the near future. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, one or more of our product candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our ongoing and planned preclinical studies and clinical trials for our viral immunotherapy programs;
- timely file and receive acceptance of our Investigational New Drug applications (INDs), in order to commence our planned clinical trials or future clinical trials;
- successfully enroll subjects in, and complete, clinical trials for our viral immunotherapy programs;
- implement measures to help minimize the risk of COVID-19 to our employees as well as patients enrolled in our clinical trials;
- timely file marketing applications and receive regulatory approvals for our product candidates from the FDA and comparable foreign regulatory authorities;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our product candidates;
- establish clinical supply capabilities through arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtain and maintain patent and trade secret protection or regulatory exclusivity for our product candidates;
- launch commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- maintain a continued acceptable safety profile of the product candidates following approval;
- obtain and maintain acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- position our products to effectively compete with other therapies;
- obtain and maintain favorable coverage and adequate reimbursement by third-party payors for our product candidates;

- enforce and defend intellectual property rights and claims with respect to our product candidates; and
- hire additional staff, including clinical, scientific and management personnel.

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 commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

***We will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.***

The development of pharmaceutical products is capital-intensive. We are currently advancing our product candidates through clinical development across a number of potential indications. We are currently conducting a Phase 3 clinical trial for CAN-2409 as first-line treatment in newly diagnosed localized prostate cancer in intermediate to high-risk patients for which we completed enrollment in September of 2021 and expect to present topline data in the fourth quarter of 2024. Our second program using CAN-2409 is for the treatment of NSCLC. We have an ongoing Phase 2 trial and initial clinical data was presented at the ASCO Annual Meeting in June 2022, and an update during our Research and Development Day in December 2022. If the final Phase 2 clinical trial is positive, this may warrant the initiation of a potentially registrational Phase 3 clinical trial. We are also studying CAN-2409 in a randomized Phase 2 clinical trial in pancreatic cancer. Consequently, we expect our expenses to significantly increase in connection with our ongoing activities, particularly as we continue our ongoing clinical trials or initiate future trials and pursue the research and development of, and seek marketing approval for, our product candidates. In addition, depending on the status of regulatory approval or, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we 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 capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts, and may be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. In March 2023, in connection with our cost management and dynamic portfolio management initiatives, we elected to pause new enrollment in this Phase 2 clinical trial, subject to additional funding. Despite this pause in patient enrollment, we continue to expect to present initial clinical data in the fourth quarter of 2023.

We expect that our existing cash and cash equivalents will be sufficient to fund our current operating plan into the second quarter of 2024. However, our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of product discovery, preclinical and clinical development, laboratory testing, manufacturing and clinical trials for the development of CAN-2409, CAN-3110, or our other potential product candidates;
- the timing of, and the costs involved in, obtaining marketing approvals for CAN-2409 in newly diagnosed localized prostate cancer, NSCLC, and pancreatic cancer as well as for CAN-3110 in our initial target indication of recurrent high-grade glioma (HGG) and our other potential product candidates that we may develop;
- if approved, the costs of commercialization activities for CAN-2409 or CAN-3110 for any approved indications or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of a collaborator that we may contract with in the future, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the potential additional expenses attributable to adjusting our development plans (including any supply related matters) to the COVID-19 pandemic;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we may enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production;
- the emergence of competing viral immunotherapies as well as immuno-oncology therapies in general and other adverse market developments;
- the costs of transitioning our clinical manufacturing operations to our new facility;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

Identifying potential product candidates and conducting preclinical development 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. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Disruptions in the financial markets in general, and more recently due to the COVID-19 pandemic, have made equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

**We have incurred indebtedness, and we may incur additional indebtedness, which could adversely affect our financial condition.**

On February 24, 2022, we entered into a loan and security agreement (the SVB Loan Agreement) with Silicon Valley Bank, as lender (SVB), pursuant to which SVB has agreed to provide term loans to us in an aggregate principal amount of up to $25.0 million. Our indebtedness could have important consequences to our stockholders. For example, it:

- increases our vulnerability to adverse general economic and industry conditions;
- limits our flexibility in planning for, or reacting to, changes in our business or the industries in which we operate by restricting our ability to make acquisitions, investments or divestments, or take other corporate actions quickly; and
- limits our ability to obtain additional financing or refinancing in the future for working capital, clinical trials, research and development, or other purposes.

Any of the above-listed factors could materially adversely affect our business, financial condition, results of operations, and cash flows. The SVB Loan Agreement also contains certain covenants, including limitations on, among other things, additional indebtedness, making certain dispositions, paying dividends in certain circumstances, and making certain acquisitions and investments. Any failure to comply with the terms, covenants and conditions of the SVB Loan Agreement may limit our ability to draw upon additional tranches of term loans and may result in an event of default

under such agreement entitling the lender to accelerate our indebtedness, which could have a material adverse effect on our business, financial condition, and results of operations.

Recent increases in interest rates have increased our borrowing costs and may also affect our ability to obtain working capital through borrowings such as bank credit lines and public or private sales of debt securities, which may result in lower liquidity, reduced working capital and other adverse impacts on our business.

A portion of our outstanding debt under the SVB Loan Agreement, bears interest at variable interest rates. To meet our liquidity needs, we have relied in part on borrowed funds with variable interest rates and may continue to do so in the future. Continued increase in interest rates may increase the cost of new indebtedness and the servicing of our outstanding indebtedness, and could materially and adversely affect our results of operations, financial condition, liquidity and cash flows.

***Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and our financial condition and results of operations.***

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (FDIC) as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of our lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. We currently have a $20 million loan outstanding pursuant to a $25 million term loan facility with SVB, which was entered into in February 2022. There can be no assurance that we will continue to have access to the balance of such loan. In addition, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. In this regard, counterparties to SVB credit agreements and arrangements, such as us, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB, and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Delayed or lost access to, or reductions in borrowings available under revolving existing credit facilities or other working capital sources and/or delays, inability or reductions in our ability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- Potential or actual breach of contractual obligations that require us to maintain letters of credit or other credit support arrangements;
- Potential or actual breach of financial covenants in our credit agreements or credit arrangements;
- Potential or actual cross-defaults in other credit agreements, credit arrangements or operating or financing agreements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our customers or suppliers, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a customer or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on us, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any customer or supplier bankruptcy or insolvency, or the failure of any customer to make payments when due, or any breach or default by a customer or supplier, or the loss of any significant supplier relationships, could result in material losses to us and may have a material adverse impact on our business.

**Risks Related to Product Development**

***Our business is dependent on the success of our lead product candidate, CAN-2409, as well as CAN-3110 and any other product candidates that we advance into the clinic. All of our product candidates will require additional development before we may be able to seek regulatory approval for and launch a product commercially.***

We currently 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 over the next several years will be devoted to our CAN-2409 program, which is currently our lead product candidate. We are currently conducting, as part of our most advanced CAN-2409 program, a Phase 3 clinical trial under an SPA for CAN-2409 as first-line neoadjuvant therapy in patients with newly diagnosed localized prostate cancer who have an intermediate to high-risk for progression. We completed enrollment for this trial in September 2021 and expect to present topline data at the end of 2024. We are conducting a Phase 2 clinical trial of CAN-2409 in patients with NSCLC who had an inadequate response to ICI and continue the same ICI in combination with CAN-2409. We presented initial clinical data from this clinical trial at the ASCO Annual Meeting in June 2022 and an update during our Research and Development Day in December 2022. We are also studying CAN-2409 in a randomized Phase 2 clinical trial in pancreatic cancer, which we elected to pause in March 2023, subject to additional funding. Additionally, we have an ongoing investigator-sponsored Phase 1 clinical trial of CAN-3110, our most advanced HSV-based product candidate, in recurrent HGG and reported additional biomarker results in November of 2021. Additional data was presented at SITC in November 2022 and during the Company's Research and Development Day on December 6, 2022. If CAN-2409, CAN-3110 or any other product candidate we develop encounters safety or efficacy issues, development delays, regulatory issues or other problems, our development plans and business would be significantly harmed. We can provide no assurance that CAN-2409, CAN-3110 or any other product candidates we develop will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of CAN-2409,

CAN-3110 or any future product candidate, or if CAN-2409, CAN-3110, or any future product candidate do not receive regulatory approval or fail to achieve significant market acceptance, we would be delayed by many years in our ability to achieve profitability, if ever.

Furthermore, even if we obtain regulatory approval for CAN-2409, CAN-3110 or any other product candidates we develop, we will still need to develop a commercial infrastructure, expand our manufacturing capabilities or develop relationships with collaborators to commercialize, establish a commercially viable pricing structure and obtain coverage and adequate reimbursement from third-party payors, including government healthcare programs. If we, or any future collaborators, are unable to successfully commercialize CAN-2409, CAN-3110 or any other product candidates we develop, we may not be able to generate sufficient revenue to continue our business.

***Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent or delay development, regulatory approval, and commercialization.***

Before obtaining regulatory approvals for the commercial sale of our product candidates, including CAN-2409, CAN-3110 or any other product candidates we develop, we must demonstrate the safety and efficacy of our product candidates for use in each target indication through lengthy, complex, and expensive preclinical studies and clinical trials. Failure can occur at any time during the preclinical study and clinical trial processes and there is a high risk of failure, so we may never succeed in developing marketable products. Any preclinical studies or clinical trials that we may conduct may not demonstrate the safety and efficacy necessary to obtain regulatory approval to market any of our product candidates. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety or efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. While we are currently in a Phase 3 clinical trial for CAN-2409 for prostate cancer and are in early stages of clinical development for CAN-3110, it is likely, as is the case with many oncology therapies, that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Our product candidates have caused side effects in clinical trials related to on-target toxicity such as fever, chills and muscle aches and other flu-like symptoms. The most common side effects observed in our clinical trials have been transient, injection site-related flu-like symptoms. The specific symptoms are largely dependent on the tumor site (site of injection). Patients who have participated in our trials have experienced grade 3 and grade 4 treatment-related side effects, including blood abnormalities. Those include pyrexia, genitourinary toxicity, increased aspartate transaminase / alanine transaminase (AST/ALT), increased bilirubin, hemiparesis, worsening of speech impairment, insomnia, headache, wound complications, empyema, motor-neuropathy symptoms/signs, transient lymphopenia, dehydration with renal insufficiency, urinary retention, worsening abdominal pain and increased lipase. Different nomenclature for the same side effect can be used in different trials (i.e. lymphopenia or low lymphocyte count). If on-target toxicity is observed at unacceptable levels, or if our product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In addition, our product candidates could cause undesirable side effects that we have not observed yet to date. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. In addition to our ongoing clinical trials of CAN-2409 and CAN-3110, patients have been, and may continue to be, treated with CAN-2409 and/or CAN-3110 under an expanded access or “compassionate use” program. To the extent the experiences of patients being treated in this program are inconsistent with or less favorable than the results of our ongoing or planned company-sponsored trials with CAN-2409 and/or CAN-3110, it may negatively affect perceptions of CAN-2409 and/or CAN-3110, our other product candidates, or our business. In addition, the FDA or comparable foreign regulatory authorities may require us to obtain and submit additional clinical data due to these inconsistent or unfavorable results, which could delay clinical development or marketing approval of CAN-2409 and/or CAN-3110 or potentially our other product candidates.

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

From time to time, we may publish interim, topline or preliminary data from our clinical trials. We may decide to conduct an interim analysis of the data after a certain number or percentage of patients have been enrolled, or after only a part of the full follow-up period but before completion of the trial. Similarly, we may report topline or preliminary results of primary and key secondary endpoints before the final trial results are completed. Preliminary, topline and interim data from our clinical trials may change as more patient data or analyses become available. Preliminary, topline or interim data from our clinical trials are not necessarily predictive of final results and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues, more patient data become available and we issue our final clinical trial report. These data 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, preliminary, interim and topline data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from more complete results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain marketing authorization for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***We may not be successful in our efforts to identify additional product candidates or indications. Due to our limited resources and access to capital, we must prioritize development of certain product candidates and indications; these decisions may prove to be wrong and may adversely affect our business.***

Although we intend to explore other therapeutic opportunities, in addition to the product candidates and indications that we are currently developing, we may fail to identify successful product candidates or additional indications for clinical development for a number of reasons. If we fail to identify additional potential product candidates or indications for development, our business could be materially harmed.
Research programs to pursue the development of our planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications and/or product candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources than we possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio.

Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. For example, at the 37th Annual Meeting of Society for Immunotherapy of Cancer (SITC) in Boston in November 2022, due to promising clinical activity of CAN-3110 in recurrent HGG, we made a portfolio and resource decision to prioritize CAN-3110 in recurrent HGG and not to pursue a Phase 3 clinical trial of CAN-2409 in HGG.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

***Results of earlier studies and trials of our product candidates may not be predictive of future trial results.***

Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having

progressed through preclinical studies and initial clinical trials. As we commence new clinical trials and continue our ongoing clinical trials, issues may arise that could suspend or terminate such clinical trials. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in clinical trials, even after positive results in earlier preclinical studies or clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Notwithstanding any potential promising results in earlier studies and trials, we cannot be certain that we will not face similar setbacks. In addition, the results of our preclinical animal studies, including our oncology mouse studies and other animal studies, may not be predictive of the results of outcomes in human clinical trials. For example, our oncology product candidates that are in preclinical development may demonstrate different chemical and biological properties in patients than they do in laboratory animal studies or may interact with human biological systems in unforeseen or harmful ways.

Additionally, some of past, ongoing and planned clinical trials utilize an “open-label” study design including our NSCLC trial in combination with ICI. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect, as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have improved notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trials when studied in a controlled environment with a placebo or active control.

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

We have concentrated our research and development efforts on our CAN-2409 and CAN-3110 product candidates, and our future success largely depends on the successful development of these therapeutic approaches. In particular, CAN-2409 utilizes an adenovirus to activate the innate and adaptive immune system. To our knowledge, there are no FDA-approved products for the treatment of cancer that utilize the adenovirus.

We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. Few viral immunotherapies have been approved globally or by the FDA to date. While the first oncolytic viral immunotherapy, talimogene laherparepvec (Imlygic, Amgen), has received FDA approval, regulatory agencies have reviewed relatively few viral immunotherapy product candidates such as CAN-2409 and CAN-3110. This may lengthen the regulatory review process, increase our development costs and delay or prevent commercialization of our product candidates. Further, any viral immunotherapies that are approved may be subject to extensive post-approval regulatory requirements, including requirements pertaining to manufacturing, distribution and promotion. We may need to devote significant time and resources to compliance with these requirements.

The FDA may also require a panel of experts, referred to as an advisory committee, to deliberate on the adequacy of the safety and efficacy data to support licensure. The opinion of the advisory committee, although not binding, may have a significant impact on our ability to obtain licensure of the product candidates based on the completed clinical trials, as the FDA often adheres to the advisory committee’s recommendations. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

In addition, our product candidates are live, gene-modified viruses for which the FDA, the EMA and other comparable foreign regulatory authorities and other public health authorities, such as the Centers of Disease Control and Prevention and hospitals involved in clinical studies, have established additional safety and contagion rules and procedures, which could establish additional hurdles for the development, manufacture or use of our vectors. These hurdles may lead to delays in the conduct of clinical trials or in obtaining regulatory approvals for further development, manufacturing or commercialization of our product candidates. We may also experience delays in transferring our process to commercial partners, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all.

Furthermore, there has been limited historical clinical trial experience for the development of products that utilize the adenovirus. Moreover, the design and conduct of our clinical trials differs from the design and conduct of previously conducted clinical trials in this area. In particular, regulatory authorities in the United States and in other jurisdictions, including Europe, have not issued definitive guidance as to how to measure and demonstrate efficacy in newly

diagnosed localized prostate cancer in intermediate- to high-risk patients in combination with the standard of care. As a result, there is substantial risk that the design or outcomes of our clinical trials will not be satisfactory to support marketing approval. For example, the endpoint in our Phase 3 clinical trial with CAN-2409 in prostate cancer is a disease-free survival (DFS) endpoint with final results expected 24 months after last patient treated, which has not been utilized in prior trials and may not be accepted by regulators as a basis for approval despite the existence of the SPA. Even if this type of novel endpoint is accepted as a basis for approval in the United States, we cannot be certain that regulators outside of the United States will accept such endpoints or will not require us to conduct additional validation studies to support the suitability of such endpoints for approval in these jurisdictions.

***We are developing, and in the future may develop, other product candidates, in combination with other therapies, which exposes us to additional risks related to any prodrugs or any agents used in combination with our product candidates.***

Our CAN-2409 product candidate is being developed to be used in combination with the prodrug valacyclovir, which is a small molecule drug marketed for treatment of herpes infections. In the future, we may develop other product candidates to be used with one or more currently approved other therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially.

If the FDA or comparable foreign regulatory authorities revoke their approval of these other drugs or revoke their approval of, or if safety, efficacy, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with any product candidate we develop, we may be unable to obtain approval.

We may also evaluate our future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market any product candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. In addition, unapproved therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delays in their clinical trials and lack of FDA approval.

***Negative developments in the field of immuno-oncology and, in particular, viral immunotherapy, could damage public perception of any of our product candidates and negatively affect our business.***

The commercial success of adenovirus- or HSV-based product candidates will depend in part on public acceptance of the use of immuno-oncology, and, in particular, viral immunotherapy. Adverse events in clinical trials of CAN-2409, CAN-3110 or any other adenovirus- or HSV-based product candidates which we may develop, or in clinical trials of others developing similar products and the resulting publicity, as well as any other negative developments in the field of immuno-oncology that may occur in the future, including in connection with competitor therapies, could result in a decrease in demand for any adenovirus- or HSV-based product candidates that we may develop. These events could also result in the suspension, discontinuation, or clinical hold of or modification to our clinical trials. If public perception is influenced by claims that the use of viral immunotherapies is unsafe, whether related to our therapies or those of our competitors, our product candidates may not be accepted by the general public or the medical community and potential clinical trial subjects may be discouraged from enrolling in our clinical trials. In addition, responses by national or state governments to negative public perception may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, prospects and results of operations and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. As a result, we may not be able to continue or may be delayed in conducting our development programs.

Our product candidates consist of modified viruses. Adverse developments in clinical trials of other immunotherapy products based on viruses, like oncolytic viruses, may result in a disproportionately negative effect for our technologies as compared to other products in the field of infectious disease and immuno-oncology that are not based on viruses. Future negative developments in the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our products. Any increased scrutiny could delay or increase the costs of obtaining marketing approval for our product candidates.

***Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.***

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment. 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 comparable foreign regulatory authorities, or as needed to provide appropriate statistical power for a given trial. In particular, because we are focused on patients with brain cancer for the development of CAN-2409 and CAN-3110 our ability to enroll eligible patients may be limited or enrollment may be slower than we anticipate due to the small eligible patient population. In addition, our ability to enroll patients may be delayed by the COVID-19 pandemic and we are unable to predict the full extent and scope of such delays.

In addition to the potentially small target populations for our planned clinical trials, particularly in brain cancer, the eligibility criteria will further limit the pool of available trial participants as we will require that patients have specific characteristics, such as a certain severity or stage of disease progression, to include them in a trial. Additionally, the process of finding eligible patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical trials because of the perceived risks and benefits of the product candidate under evaluation, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients, the availability of genetic sequencing information for patient tumors so that we can identify patients with the targeted genetic mutations, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed. The enrollment of patients further depends on many factors, including:

- the proximity of patients to clinical trial sites;
- patient referral practices of physicians;
- the design of the clinical trial, including the number of site visits and invasive assessments required;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- reporting of the preliminary results of any of our clinical trials;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion; and
- factors we may not be able to control, such as the COVID-19 pandemic, that may limit patient participation, hiring of principal investigators or staff or clinical site availability.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because certain of our product candidates represent a departure from more commonly used methods for cancer treatment and because certain of our product candidates have not been tested in humans before, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in any future clinical trial of our product candidates.

***If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented.***

Even if we receive marketing approval for our current or future product candidates, our current or future product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.

The commercial success of our current or future product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our current or future product candidates among the medical community, including physicians, patients and healthcare payors. Market acceptance of our current or future product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy of our current or future product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared to other available medicines;

- limitations or warnings contained in the labeling approved for our current or future product candidates by the FDA or other applicable regulatory authorities;
- the prevalence and severity of adverse events associated with our product candidates or those products with which they may be co-administered in immuno-oncology and, in particular, viral immunotherapies;
- the clinical indications for which our current or future product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages of our current or future product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the willingness of the target patient populations to try new therapies or treatment methods and of physicians to prescribe these therapies or methods in immuno-oncology and, in particular, viral immunotherapies;
- the need to dose such product candidates in combination with other therapeutic agents, and related costs;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of our current or future product candidates;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the ability or willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- potential product liability claims.

If our current or future product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our current or future product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our current or future product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community, patient organizations and third-party payors about the benefits of our current or future product candidates may require significant resources and may never be successful.

***We face substantial competition, which may result in others discovering, developing or commercializing product candidates before or more successfully than we do.***

The development and commercialization of new product candidates is highly competitive. We face competition from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others with respect to CAN-2409 and CAN-3110 and will face similar competition with respect to any product candidates that we may seek to develop or commercialize in the future. We compete in pharmaceutical, biotechnology and other related markets that develop immuno-oncology therapies for the treatment of cancer. There are other companies working to develop viral immunotherapies for the treatment of cancer including divisions of large pharmaceutical and biotechnology companies of various sizes. The large pharmaceutical and biotechnology companies that have commercialized and/or are developing immuno-oncology treatments for cancer include AstraZeneca, Bristol-Myers Squibb, Gilead Sciences, Merck, Novartis, Pfizer, Regeneron and Roche/Genentech.

Some of the products and therapies developed by our competitors are based on scientific approaches that are the same as or similar to our approach, including with respect to the use of viral immunotherapy with adenovirus and HSV. Other competitive products and therapies are based on entirely different approaches. We are aware that Oncorus, Replimune, Amgen, ImmaVira, FerGene and IconOVir, among others, are developing viral immunotherapies that may have utility for the treatment of indications that we are targeting. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of the companies we compete against or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in concentration of even more resources among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly

through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, in establishing clinical trial sites and enrolling subjects for our clinical trials and in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination of our commercial opportunity if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, or are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or foreign 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 we are able to enter the market. The key competitive factors affecting the success of all our product candidates, if approved, are likely to be their efficacy, safety, convenience and price, if required, the level of biosimilar or generic competition and the availability of reimbursement from government and other third-party payors.

**Risks Related to Government Regulation and Commercialization of Our Product Candidates**

***The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or experience delays in obtaining, required regulatory approvals, we will not be able to commercialize CAN-2409, CAN-3110 and future product candidates as expected, and our ability to generate revenue may be materially impaired.***

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. These regulatory requirements may require us to amend our clinical trial protocols, including to comply with the protocols of any applicable SPA we receive from the FDA; conduct additional preclinical studies or clinical trials that may require regulatory or independent IRB approval; or otherwise cause delays in obtaining approval or rejection of an application. Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to generate revenue from the particular product candidate, which may materially harm our business, financial condition, results of operations, stock price and prospects.

Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. The number and types of preclinical studies and clinical trials that will be required for regulatory approval also varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. 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, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, any of which may cause delays or limitations in the approval or a decision not to approve an application. It is possible that CAN-2409, CAN-3110 and future product candidates will never obtain the appropriate regulatory approvals necessary for us to commence product sales.

If we experience delays in obtaining approval, if we fail to obtain regulatory approval of CAN-2409, CAN-3110 or any future product candidate or if the label for a product candidate does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, the commercial prospects for such product candidate may be harmed and our ability to generate revenues from that product candidate may be materially impaired.

CAN-2409, CAN-3110 or future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any. Serious adverse events or undesirable side effects caused by CAN-2409, CAN-3110 and future product candidates could cause us, IRBs, and other reviewing entities or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. For example, if concerns are raised regarding the safety of a new therapeutic as a result of undesirable side effects identified during clinical or preclinical testing, the FDA or comparable foreign regulatory authority may order us to cease further development, decline to approve the product candidate or issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve the product candidate. The FDA or comparable foreign regulatory authorities, or IRBs and other reviewing entities, may also require, or we may voluntarily develop, strategies for managing adverse events during clinical development, which could include restrictions on our enrollment criteria, the use of stopping criteria, adjustments to a study's design, or the monitoring of safety data by a data monitoring committee, among other strategies. For example, patients enrolled in our ongoing clinical trials of CAN-2409 and CAN-3110 have experienced mild to moderate adverse events, consisting mainly of flu-like symptoms and injection site reactions. In response to these adverse events, we have implemented prophylactic measures, including intravenous fluids, antiemetics and

antipyretics. The FDA's or a comparable foreign regulatory authority's requests for additional data or information could also result in substantial delays in the approval of CAN-2409, CAN-3110 and future product candidates.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of a product candidate may only be uncovered when a significantly larger number of patients are exposed to the product candidate or when patients are exposed for a longer period of time.

Undesirable side effects caused by CAN-2409, CAN-3110 or any future product candidates could also result in denial of regulatory approval by the FDA or comparable foreign regulatory authorities for any or all targeted indications or the inclusion of unfavorable information in our product labeling, such as limitations on the indicated uses for which the products may be marketed or distributed, a label with significant safety warnings, including boxed warnings, contraindications, and precautions, a label without statements necessary or desirable for successful commercialization, or may result in requirements for costly post-marketing testing and surveillance, or other requirements, including the submission of a Risk Evaluation and Mitigation Strategy or REMS, to monitor the safety or efficacy of the products, and in turn prevent us from commercializing and generating revenues from the sale of CAN-2409, CAN-3110 and future product candidates. Any such limitations or restrictions could similarly impact any supplemental marketing approvals we may obtain for CAN-2409 and CAN-3110. Undesirable side effects may limit the potential market for any approved products or could result in restrictions on manufacturing processes, the discontinuation of the sales and marketing of the product, or withdrawal of product approvals. We could also be sued and held liable for harm caused to patients, or become subject to fines, injunctions or the imposition of civil or criminal penalties.

If CAN-2409, CAN-3110 and future product candidates are associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The therapeutic-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may materially harm our business, financial condition, results of operations, stock price and prospects.

***The FDA's agreement to a Special Protocol Assessment with respect to the study design of our Phase 3 clinical trial of CAN-2409 in newly diagnosed localized prostate cancer in intermediate and high-risk patients does not guarantee any particular outcome from regulatory review, including ultimate approval, and may not lead to a successful review or approval process.***

We have obtained agreement from the FDA on the design and size of our Phase 3 clinical trial of CAN-2409 in newly diagnosed localized prostate cancer in intermediate- and high-risk patients in combination with the standard of care through an SPA. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs and biologics by allowing the FDA to evaluate the proposed design and size of certain clinical or animal studies, including clinical trials that are intended to form the primary basis for determining a product candidate's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. The FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design of the trial, such as entry criteria, dose selection, endpoints and/or planned analyses, are acceptable to support regulatory approval of the product with respect to the effectiveness of the indication studied. All exchanges between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA may agree to an SPA, an SPA agreement does not guarantee approval of a product. Even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. While we have obtained an SPA agreement for our Phase 3 clinical trial, we have subsequently made minor amendments to the protocol and have not obtained an SPA amendment in connection with the amended protocol.

In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval of CAN-2409 in prostate cancer.

***A fast track designation by the FDA, even though granted for CAN-2409, or if received for any other future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.***

If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA fast track designation for a particular indication. We have been granted fast track designation for the use of CAN-2409 for the treatment of localized, primary prostate cancer in combination with radiation therapy to improve the local control rate and may seek fast track designation for CAN-3110 or certain of our future product candidates. However, there is no assurance that the FDA will grant this status to CAN-3110 or any of our proposed product candidates. Marketing applications filed by sponsors of products in fast track development may qualify for priority review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even though we have received fast track designation for CAN-2409 or if we do receive fast track designation for CAN-3110 or any other of our future product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any fast track designation at any time.

***A breakthrough therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.***

We may seek breakthrough therapy designation for some or all of our future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Sponsors of product candidates that have been designated as breakthrough therapies are eligible to receive more intensive FDA guidance on developing an efficient drug development program, an organizational commitment involving senior managers, and eligibility for rolling review and priority review. Drugs and biologics designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates developed and considered for approval that have not received breakthrough therapy designation and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification. Thus, even though we may seek breakthrough therapy designation for CAN-2409, CAN-3110 or some or all of our future product candidates for the treatment of various cancers, there can be no assurance that we will receive breakthrough therapy designation.

***Accelerated approval by the FDA, even if granted for certain of our current or future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.***

We may seek approval of certain of our current or future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence by the sponsor and, under the Food and Drug Omnibus Report Act of 2022 (FDORA), the FDA is permitted to require, as appropriate, that such trials be underway prior to approval or within a specified time period after the date accelerated approval is granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such confirmatory trials, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such trials in a

timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory trial or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance that the product's accelerated approval will eventually be converted to a traditional FDA approval.

***Even if our development efforts are successful, we may not obtain regulatory approval of CAN-2409, CAN-3110 or any future product candidates in the United States or other jurisdictions, which would prevent us from commercializing CAN-2409, CAN-3110 and future product candidates. Even if we obtain regulatory approval for CAN-2409, CAN-3110 and future product candidates, any such approval may be subject to limitations, including with respect to the approved indications or patient populations, which could impair our ability to successfully commercialize CAN-2409, CAN-3110 or any future product candidates.***

We are not permitted to market or promote or sell CAN-2409, CAN-3110 or any future product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities and clinical trial sites by, the regulatory authorities. If we do not receive approval from the FDA and comparable foreign regulatory authorities for any of CAN-2409, CAN-3110 and future product candidates, we will not be able to commercialize such product candidates in the United States or in other jurisdictions. If significant delays in obtaining approval for and commercializing CAN-2409, CAN-3110 and future product candidates occur in any jurisdictions, our business, financial condition, results of operations, stock price and prospects will be materially harmed. Even if CAN-2409, CAN-3110 and future product candidates are approved, they may:

- be subject to limitations on the indicated uses or patient populations for which they may be marketed, distribution restrictions, or other conditions of approval;
- not be approved with label statements necessary or desirable for successful commercialization; or
- contain requirements for costly post-market testing and surveillance, or other requirements, including the submission of a REMS, to monitor the safety or efficacy of the products.

We have not previously submitted a Biologics License Application (BLA), to the FDA, or a similar marketing application to comparable foreign regulatory authorities, for CAN-2409, CAN-3110 or any product candidate, and we can provide no assurance that we will ultimately be successful in obtaining regulatory approval for claims that are necessary or desirable for successful marketing, if at all.

***Changes in product candidate manufacturing or formulation may result in additional costs or delay.***

As product candidates are developed through preclinical studies to later-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Any of these changes could cause CAN-2409, CAN-3110 or any future product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Changes in third-party manufacturers and manufacturing processes may also require additional testing, or notification to, or approval by the FDA or a comparable foreign regulatory authority. Such changes could be further delayed due to development of clinical-scale manufacturing and commercial-scale manufacturing operations. This could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of CAN-2409, CAN-3110 and future product candidates and jeopardize our ability to commence product sales and generate revenue.

***Inadequate funding for the FDA, the SEC and other government agencies 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 agency have fluctuated in recent years as a result. 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 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. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown 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. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, since March, 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and that a remote interactive evaluation is not adequate, the FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. 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.

***Even if CAN-2409, CAN-3110 or any future product candidates receive regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense and limit how we manufacture and market our products.***

Any product candidate for which we may obtain marketing approval will be subject to extensive and ongoing requirements of and review by the FDA and comparable foreign regulatory authorities, including requirements related to the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising, marketing, and promotional activities for such product. These requirements further include submissions of safety and other post-marketing information, including manufacturing deviations and reports, registration and listing requirements, the payment of annual fees, continued compliance with current good manufacturing practice (cGMP), requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents, and good clinical practices (GCPs), for any clinical trials that we conduct post-approval.

The FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of CAN-2409, CAN-3110 and future product candidates, they may withdraw approval, issue public safety alerts, require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. Any such restrictions could limit sales of the product.

We and any of our suppliers or collaborators, including our CMOs, could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs and other FDA regulatory requirements. Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. Application holders must further notify the FDA, and depending on the nature of the change, obtain FDA pre-approval for product and manufacturing changes.

In addition, later discovery of previously unknown adverse events or that the product is less effective than previously thought or other problems with any products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements both before and after approval, may yield various negative results, including:

- restrictions on manufacturing, distribution, or marketing of such products;
- restrictions on the labeling, including required additional warnings, such as boxed warnings, contraindications, precautions, and restrictions on the approved indication or use;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;

- modifications to promotional pieces;
- issuance of corrective information;
- requirements to conduct post-marketing studies or other clinical trials;
- clinical holds or termination of clinical trials;
- requirements to establish or modify a REMS or similar strategy;
- changes to the way the product is administered to patients;
- liability for harm caused to patients or subjects;
- reputational harm;
- the product becoming less competitive;
- warning or untitled letters;
- suspension of marketing or withdrawal of the products from the market;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recalls of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention;
- FDA debarment, suspension and debarment from government contracts, and refusal of orders under existing government contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements; or
- injunctions or the imposition of civil, criminal or administrative penalties, including imprisonment.

Any of these events could prevent us from achieving or maintaining market acceptance of any particular product or could substantially increase the costs and expenses of commercializing such product, which in turn could delay or prevent us from generating significant revenues from its marketing and sale. Any of these events could further have other material and adverse effects on our operations and business and could adversely impact our business, financial condition, results of operations, stock price and prospects.

Further, the FDA's policies or those of comparable foreign regulatory authorities may change and could impose extensive and ongoing regulatory requirements and obligations on any product candidate for which we obtain marketing approval. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and be subject to regulatory enforcement action, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

***Regulatory approval by the FDA or comparable foreign regulatory authorities is limited to those specific indications and conditions for which approval has been granted, and we may be subject to substantial fines, criminal penalties, injunctions or other enforcement actions if we are determined to be promoting the use of our products for unapproved or "off-label" uses, or in a manner inconsistent with the approved labeling, resulting in damage to our reputation and business.***

We must comply with requirements concerning advertising and promotion for any product candidates for which we obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, Department of Justice, the Office of Inspector General for the Department of Health and Human Services (HHS), state attorneys general, members of Congress and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved. If we are not able to obtain FDA approval for desired uses or indications for CAN-2409, CAN-3110 and future product candidates, we may not market or promote them for those indications and uses, referred to as off-label uses, and our business, financial condition, results of operations, stock price and prospects will be materially harmed. We also must sufficiently

substantiate any claims that we make for any products, including claims comparing those products to other companies' products, and must abide by the FDA's strict requirements regarding the content of promotion and advertising.

Physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off-label use.

If we are found to have impermissibly promoted any of CAN-2409, CAN-3110 and future product candidates, we may become subject to significant liability and government fines. The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. In the United States, engaging in the impermissible promotion of any products, following approval, for off-label uses can also subject us to false claims and other litigation under federal and state statutes. These include fraud and abuse and consumer protection laws, which can lead to civil and criminal penalties and fines, agreements with governmental authorities that materially restrict the manner in which we promote or distribute therapeutic products and conduct our business. These restrictions could include corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, and suspension and debarment from government contracts and refusal of orders under existing government contracts. These False Claims Act lawsuits against manufacturers of drugs and biologics have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements pertaining to certain sales practices and promoting off-label uses. In addition, False Claims Act lawsuits may expose manufacturers to follow-on claims by private payers based on fraudulent marketing practices. This growth in litigation has increased the risk that a biopharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, as well as criminal and civil penalties, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we do not lawfully promote our approved products, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations, stock price and prospects.

In the United States, the promotion of biopharmaceutical products is subject to additional FDA requirements and restrictions on promotional statements. If, after CAN-2409, CAN-3110 or any future product candidates obtains marketing approval, the FDA determines that our promotional activities violate its regulations and policies pertaining to product promotion, it could request that we modify our promotional materials or subject us to regulatory or other enforcement actions, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, requests for recalls, payment of civil fines, disgorgement of money, imposition of operating restrictions, injunctions or criminal prosecution, and other enforcement actions. Similarly, industry codes in foreign jurisdictions may prohibit companies from engaging in certain promotional activities, and regulatory agencies in various countries may enforce violations of such codes with civil penalties. If we become subject to regulatory and enforcement actions, our business, financial condition, results of operations, stock price and prospects will be materially harmed.

***We may not be able to file INDs or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or a comparable foreign regulatory may not permit us to proceed.***

The FDA or comparable foreign regulatory authorities may require us to file separate INDs for additional clinical trials we plan to conduct with our current lead product candidates, CAN-2409 and CAN-3110. We may not be able to file any additional INDs required for our current product candidates and any future product candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies, including due to the impact of the COVID-19 pandemic on suppliers, study sites or third-party contractors and vendors on whom we depend. We may also experience delays if we are unable to access earlier data from inactive or withdrawn INDs. Moreover, we cannot be sure that submission of an IND will result in the FDA or comparable foreign regulatory authorities allowing further clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the expected timelines to obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all. There are similar risks related to the review and authorization of our protocols and amendments by comparable foreign regulatory authorities.

***If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.***

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated approval pathway for biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the other company's product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened or unavailable due to congressional action, a determination that approval of one of our candidates does not constitute "first licensure" or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

***The size of the potential market for our product candidates is difficult to estimate and, if any of our assumptions are inaccurate, the actual markets for our product candidates may be smaller than our estimates.***

Our current and future target patient populations are based on our beliefs and estimates regarding the incidence or prevalence of certain types of the indications that may be addressable by our product candidates, which is derived from a variety of sources, including scientific literature and surveys of clinics. Our projections may prove to be incorrect and the number of potential patients may turn out to be lower than expected. The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access, the success of competing therapies and product pricing and reimbursement. Further, the market opportunity for viral immunotherapies is hard to estimate given that it is an emerging field with few globally or FDA-approved therapies, none of which have yet to enjoy broad market acceptance. Even if we obtain significant market share for our product candidates, because the potential target populations could be small, we may never achieve profitability without obtaining regulatory approval for additional indications.

***Healthcare reform measures may have a material adverse effect on our business and results of operations.***

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current or future product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Among policy-makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

***If, in the future, we are unable to establish sales and marketing and patient support capabilities or enter into agreements with third parties to sell and market our current or future product candidates, we may not be successful in commercializing our current or future product candidates if and when they are approved, and we may not be able to generate any revenue.***

We do not currently have a sales or marketing infrastructure and have limited experience in the sales, marketing, patient support or distribution of products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, patient support, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our current or future product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing and patient support capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any drug 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. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to use any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing, patient support and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any current or future product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our current or future product candidates or may be unable to do so on terms that are favorable 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 current or future product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our current or future product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

***If any product candidate for which we receive regulatory approval does not achieve broad market acceptance among physicians, patients, healthcare payors, and the medical community, the revenues that we generate from its sales will be limited.***

Even if our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors, and others in the medical community. Commercial success also will depend, in large part, on the coverage and reimbursement of our product candidates by third-party payors, including private insurance providers and government payors. The degree of market acceptance of any approved product would depend on a number of factors, including:

- the efficacy, safety and tolerability as demonstrated in clinical trials;
- the timing of market introduction of such product candidate as well as competitive products;
- the clinical indications for which the product is approved;
- acceptance by physicians, major operators of cancer or neurology clinics and patients of the product as a safe, tolerable and effective treatment;
- the potential and perceived advantages of the product candidate over alternative treatments;
- the safety and tolerability of the product candidate in a broader patient group;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate reimbursement by third party payors and government authorities;
- changes in regulatory requirements by government authorities for the product candidate;
- relative convenience and ease of administration;
- the prevalence and severity of side effects and adverse events;
- the effectiveness of our sales and marketing efforts; and
- favorable or unfavorable publicity relating to the product or relating to the Company.

Our ability to successfully launch and secure market acceptance of our late-stage pipeline candidate, CAN-2409 (if approved), may be impacted by the evolving COVID-19 pandemic, although we are currently unable to predict or quantify any such potential impact with any degree of certainty. If the spread of COVID-19 and the social distancing measures taken by various governments continue, any commercial launch we may undertake may be hindered by various factors, including challenges in hiring the employees necessary to support commercialization; delays in demand due to impacts on the healthcare system and overall economy; delays in coverage decisions from Medicare and third-party payors; restrictions on our personal interactions with physicians, hospitals, payors, and other customers; interruptions or delays in our commercial supply chain; and increases in the number of uninsured or underinsured patients.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate sufficient revenue from these products and we may not become profitable, which would have a material adverse effect on our business.

***If we fail to develop additional product candidates, our commercial opportunity could be limited.***

We expect initially to develop our lead product candidates, CAN-2409 and CAN-3110. A key part of our strategy, however, is to pursue clinical development of additional product candidates. Developing, obtaining marketing approval for, and commercializing additional product candidates will require substantial additional funding and will be subject to the risks of failure inherent in medical product development. We cannot assure you that we will be able to successfully advance any of these additional product candidates through the development process.

Even if we obtain approval from the FDA or comparable foreign regulatory authorities to market additional product candidates for the treatment of solid tumors, we cannot assure you that any such product candidates will be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize additional product candidates our commercial opportunity may be limited and our business, financial condition, results of operations, stock price and prospects may be materially harmed.

***Our relationships with customers 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 criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.***

Although we do not currently have any drugs on the market, if we begin commercializing our current or future product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers,

physicians and third-party payors play a primary role in the recommendation and prescription of any current or future product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable 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 our current or future product candidates for which we obtain marketing approval.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge and may not comply under one or more of such laws, regulations and guidance. Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do 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, including anticipated activities to be conducted by our sales team, were to be 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 administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results.

***We may face potential liability if we obtain identifiable patient health information from clinical trials sponsored by us.***

Most healthcare providers, including certain research institutions from which we may obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, in the future, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who may enroll in patient assistance programs if we choose to implement such programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

Foreign data protection laws, including the European Union's General Data Protection Regulation (the EU GDPR), and the United Kingdom (or UK) equivalent of the same (the UK GDPR, together with the EU GDPR, the GDPR) may also apply to our processing of health-related and other personal data.

The GDPR imposes stringent requirements for controllers and processors of personal data of individuals within the European Economic Area, or EEA, or the UK. The GDPR applies to any company established in the EEA or UK as well as to those outside the EEA or UK if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or UK or the monitoring of their behavior. The GDPR, together with national legislation, regulations and guidelines of the EEA Member States and the UK governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA or the UK, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for breaches of the data protection obligations. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million (£17.5 million) or 4% of the annual global revenues of the noncompliant company, whichever is greater. Currently, the EU GDPR and UK GDPR remain largely aligned, but the UK has announced plans to reform the country's data protection legal framework in its Data Reform Bill, which will introduce significant changes from the EU GDPR. This may lead to additional compliance costs and could increase our overall risk exposure as we may no longer be able to take a unified approach across the EEA and the UK, and we will need to amend our processes and procedures to align with the new framework.

The GDPR also imposes restrictions in relation to the international transfer of personal data from the EEA and UK and other countries in respect of which the European Commission or the UK government has not issued a so-called "adequacy decision" or " adequacy regulation" (known as "third countries"), unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. This includes putting in place the European

Commission's Standard Contractual Clauses for transfers outside of the EEA and a similar transfer mechanism for transfers of personal data outside of the UK, the International Data Transfer Agreement or Addendum (IDTA). Under both the EU GDPR and the UK GDPR, exporters are also required to assess the risk of the data transfer on a case-by-case basis, including an analysis of the laws in the destination country. The EU Standard Contractual Clauses had to be in place by December 27, 2022, whereas the IDTA must be implemented in all existing contracts March 21, 2024. Finalizing the implementation of the updated Standard Contractual Clauses and UK IDTA, and conducting the required risk assessments, may continue to necessitate significant contractual overhaul of our data transfer arrangements with customers, sub-processors and vendors.

Implementing mechanisms to endeavor to ensure compliance with the GDPR and relevant local legislation in EEA Member States and the UK may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations, and prospects. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, and orders to cease/change our use of data, enforcement notices, or potential civil claims including class action-type litigation.

In addition, governments in the United States are increasingly passing stringent privacy laws. California recently enacted and has proposed companion regulations to the California Consumer Privacy Act (CCPA), which went into effect January 1, 2020. The CCPA creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. As of March 28, 2020, the California State Attorney General has proposed varying versions of companion draft regulations which are not yet finalized. Despite the delay in adopting regulations, the California State Attorney General commenced enforcement actions against violators on July 1, 2020. While there are currently exceptions for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. On August 14, 2020, implementing regulations were finalized and became effective as of that date. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope. We continue to monitor the impact the CCPA may have on our business activities.

Additionally, a new California ballot initiative, the California Privacy Rights Act (CPRA) was passed in November 2020. Effective starting on January 1, 2023, the CPRA imposes additional obligations on companies covered by the legislation and will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The effects of the CCPA and the CPRA are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and/or litigation.

Also, on March 2, 2021, Virginia enacted the Consumer Data Protection Act (CDPA). The CDPA will become effective January 1, 2023. The CDPA will regulate how businesses, which the CDPA refers to as "controllers", collect and share personal information. The law applies to companies that conduct business in Virginia or product products or services that are targeted to residents of Virginia and either: (1) annually control or process personal data of at least 100,000 Virginia residents; or (2) control or process the personal data of at least 25,000 Virginia residents and derive over 50% of gross revenue from the sale of personal data. While the CDPA incorporates many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of controllers. The new law will impact how controllers collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests. In addition, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act (CPA) into law. The CPA is rather similar to the Virginia's CPDA but also contains additional requirements. The new measure applies to companies conducting business in Colorado or who produce or deliver commercial products or services intentionally targeted to its residents of the state and that either: (1) control or process the personal data of at least 100,000 Colorado residents during a calendar year; or (2) derive revenue or receive a discount on the price of goods or services from the sale of personal data and process or control the personal data of at least 25,000 Colorado residents.

Moreover, on March 24, 2022, Utah's governor signed the Utah Consumer Privacy Act (UCPA) into law. The UCPA will take effect on December 31, 2023. Also, in May 2022, Connecticut Governor Lamont signed the Connecticut Data Privacy Act (CTDPA) into laws. The UCPA and CTDPA draw heavily upon their predecessors in Virginia and Colorado. With the CTDPA, Connecticut became the fifth state to enact a comprehensive privacy law. New privacy and data security laws have been proposed in more than half of the states in the U.S. and in the U.S. Congress. With bills proposed in many other jurisdictions, it remains quite possible that other states will follow suit. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The

existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

The increasing number and complexity of regional, country and U.S. state data protection laws, and other changes in laws or regulations across the globe, especially those associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations

Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators may obtain health information, as well as the providers who may share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party contract research organizations (CROs) or other contractors or consultants fail to comply with applicable federal, state/provincial or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our therapeutics. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage.

Additionally, we are subject to other state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, 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 connection with our storage or disposal of biological, hazardous or radioactive materials.

**Risks Related to Employee Matters, Managing Growth and General Business Operations**

***The COVID-19 pandemic may affect our ability to complete our ongoing clinical trials and initiate and complete other preclinical studies, planned clinical trials or future clinical trials, disrupt regulatory activities, disrupt our manufacturing and supply chain or have other adverse effects on our business and operations. In addition, this pandemic caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.***

The COVID-19 pandemic caused many governments to implement measures to slow the spread of COVID-19 through quarantines, travel restrictions, heightened border scrutiny and other measures. The COVID-19 pandemic and government measures taken in response also had a significant impact, both directly and indirectly, on businesses and commerce, as worker shortages occurred; supply chains have been disrupted; facilities and production were suspended; and demand for certain goods and services, such as medical services and supplies, spiked, while demand for other goods and services, such as travel, fell. While the impact of the COVID-19 pandemic on our operations, including, among others, our manufacturing and supply chain, sales and marketing, commercial and clinical trial operations, to date has not been material, the future progression of the COVID-19 pandemic and its effects on our business and operations are uncertain.

The extent to which COVID-19 had and may in the future have an impact on our operations or those of the third parties on which we rely depends on many factors, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, any future variants of COVID-19, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19, and the actions to contain the COVID-19 pandemic or address its impact in the short and long term. Additionally, the conduct of our clinical trials, preclinical studies and manufacturing activities is dependent upon the availability of clinical trial sites, CROs, CMOs, researchers and investigators, regulatory agency personnel and logistics providers, all of which may in the future be adversely affected by the COVID-19 pandemic.

Any negative impact that the COVID-19 pandemic may have on enrolling or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause delays with respect to product development activities, which could materially and adversely affect our ability to obtain marketing approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results.

***We cannot provide assurance that some factors from the COVID-19 pandemic will not further delay or otherwise adversely affect our clinical development, research, manufacturing and business operations activities, as well as our business generally, in the future.***

We and the third-party manufacturers, CROs and academic collaborators that we engage have faced in the past and may face in the future disruptions that could affect our ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates, laboratory supplies for our preclinical studies and clinical trials, or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic. For example, during the COVID-19, there were global supply chain disruptions, particularly with raw materials and supplies used in biopharmaceutical production. Several vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA, and more may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. Additionally, the response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to pursue marketing approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and potential approvals due to measures intended to limit in-person interactions.

In response to the COVID-19 pandemic and in accordance with direction from state and local governmental authorities, we carefully monitored the COVID-19 pandemic and its impact on our business and took important steps to help ensure the safety of our employees and their families and to reduce the spread of COVID-19. We established a flexible work policy for our employees under which we encourage all of our employees to work from the office or from home as they feel appropriate. Those employees performing or supporting business-critical operations, such as members of our laboratory and facilities staff, are working on site at our facilities on a daily basis. For those employees who come to work at our facilities, we have implemented stringent safety measures designed to comply with applicable federal, state and local guidelines instituted in response to the COVID-19 pandemic. We have taken these precautionary steps while maintaining business continuity so that we can continue to progress our programs. In the event that governmental authorities were to impose new restrictions, our employees conducting research and development activities may not be able to access our laboratory space, and our core research activities may be significantly limited or curtailed, possibly for an extended period of time.

The extent of any future impact of COVID-19 to our business, preclinical studies and clinical trials will depend on future developments, which are uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the COVID-19 pandemic, travel restrictions and actions to contain the COVID-19 pandemic, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The COVID-19 pandemic caused significant disruptions in the financial markets, and may cause disruptions in the future, which could adversely impact our ability to raise additional funds through public offerings or private placements and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the COVID-19 pandemic could impact economies worldwide in the future, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations and prospects.

***Our future success depends on our ability to retain key executives 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 have entered into employment agreements with 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 will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, 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 pharmaceutical and biotechnology 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 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. 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, manufacturing 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.***

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities. We expect the number of our employees and the scope of our operations to grow, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate 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. 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. The expansion of our operations may 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.

***The increasing use of social media platforms presents new risks and challenges.***

Social media is increasingly being used to communicate about our clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of our product candidates, if any. Social media practices in the biotechnology and biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities and heightened scrutiny by the FDA, the SEC and other regulators. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, product candidates or products. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

***Our internal computer systems, or those of our third-party CROs that we may use in the future, or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs.***

Despite our implementation of security measures, our internal computer systems, and those of our CROs that we may use in the future, information technology suppliers and other contractors and consultants are vulnerable to damage from computer viruses, cyberattacks and other unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it

could result in a material disruption of our product candidate development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of any of our product candidates could be delayed. In addition, our liability and cyber insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks or other related liabilities.

Cyberattacks are increasing in their frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. They are often carried out by well-resourced and skilled parties, including nation states, organized crime groups, “hacktivists” and employees or contractors acting carelessly or with malicious intent. Cyber-attacks include deployment of harmful malware and key loggers, ransomware, denial-of-service attacks, malicious websites, the use of social engineering, and other means to affect the confidentiality, integrity and availability of our technology systems and data. Cyber-attacks also include manufacturing, hardware or software supply chain attacks, which could cause a delay in the manufacturing of products or products produced for contract manufacturing or lead to a data privacy or security breach. Our business partners face similar risks, and any security breach of their systems could adversely affect our security. In addition, our increased use of cloud technologies heightens these third party and other operational risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber-attacks could disrupt our operations and result in misappropriation, corruption, or loss of confidential or propriety information. Risk of cyber-attack is increased with employees working remotely. Remote work increases the risk we may be vulnerable to cybersecurity-related events such as phishing attacks and other security threats.

***Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic, war or other catastrophic event.***

We depend on our employees and consultants, CDMOs and CROs that we may use in the future, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attacks, pandemics, wars hurricanes, fire, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such as natural disasters, the outbreak of war, the escalation of hostilities and acts of terrorism or other “acts of God,” particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. For example, in late February 2022, Russian military forces launched significant military action against Ukraine, and sustained conflict and disruption in the region is likely. The impact to Ukraine, as well as actions taken by other countries, including new and stricter sanctions by Canada, the United Kingdom, the European Union, the United States and other countries and organizations against officials, individuals, regions, and industries in Russia, Ukraine and Belarus, and each country’s potential response to such sanctions, tensions, and military actions could have an adverse effect on the Company’s operations. These countries may impose further sanctions or other restrictive actions against governmental or other individuals or organizations in Russia or elsewhere. The effects of disruptive events could affect the global economy and financial and commodities markets in ways that cannot necessarily be foreseen at the present time. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not respond or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CDMOs or CROs, regulatory agencies or other parties with which we are engaged could have a significant negative impact on our operations and financial performance.

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

As a public company, we are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make a required related party transaction disclosure. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

***We and our independent registered public accounting firm identified material weaknesses in our internal control over financial reporting in conjunction with their audits of our financial statements for the years ended***

***December 31, 2021 and 2020. Those material weaknesses were subsequently remediated in 2022. If we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business and the market price of our common stock.***

We are subject to the requirements of the Sarbanes-Oxley Act and the applicable SEC rules and regulations that require an annual management report on our internal control over financial reporting. In preparation of our consolidated financial statements for the years ended December 31, 2021 and 2020, we and our independent registered public accounting firm identified material weaknesses in our internal control over financial reporting. Those material weaknesses were subsequently remediated as of December 31, 2022. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

These previously identified material weaknesses related to:

1. not having sufficient finance and accounting staff with U.S. generally accepted accounting principles (GAAP) technical and accounting expertise to evaluate and account for significant transactions and oversee our third-party consultants. As a result we did not design and maintain formal accounting policies, processes and controls to analyze, account for and disclose certain complex transactions, which led to inappropriate accounting conclusions associated with stock compensation expenses; and
2. the lack of proper monitoring entity level controls and segregation of duties due to our small accounting staff.

We implemented measures designed to improve internal control over financial reporting, which resulted in the remediation of the control deficiencies that led to these material weaknesses, including the following:

- hired a new Chief Financial Officer in September 2022 with prior experience serving as a chief financial and accounting officer of several public companies who also served ten years in a major public accounting firm. We hired a Controller in November 2021 with experience working at a public company and as a manager at a major public accounting firm. Each of the above personnel have technical accounting expertise and experience with the internal control, compliance, and financial reporting requirements of companies subject to Public Company Accounting Oversight Board (PCAOB) standards;
- strengthened supervisory reviews by our financial management;
- expanded our accounting and finance team to add additional qualified accounting and finance resources, which included augmenting our finance team with third-party consultants that possessed the required expertise to assist management with their review.
- implemented Oracle NetSuite as our Enterprise Resource Planning (ERP) solution in the third quarter of 2022, which among other features, has automated segregation of duties functionality relating to the ability to create and post journal entries to our general ledger;
- implemented a SAAS solution to assist with the review and approval of account reconciliations and other financial close workflows;
- enhanced business process narratives and identification of key controls in our Sarbanes-Oxley Act (SOX Act) framework; and
- performed internal interim and year-end SOX assessments that did not result in the identification of any material weaknesses related to the design or operating effectiveness of identified key controls.

We cannot assure you that we will not identify additional material weaknesses in our internal control over financial reporting. In addition, our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting in accordance with the provisions of the SOX Act because no such evaluation has been required. Had our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the SOX Act, one or more material weaknesses may have been identified. If future material weaknesses are identified in our internal control over financial reporting, or if we otherwise fail to maintain an effective system of internal controls, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and the market price of our common stock may decline as a result.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.***

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management are required to assess the effectiveness of these controls annually. However, for as long as we are an EGC under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five years. Our assessment of internal controls and procedures may not detect material weaknesses in our internal control over financial reporting. Material weaknesses in our internal control over financial reporting may go undetected and could lead to financial statement restatements and require us to incur the expense of remediation, which could have a negative effect on the trading price of our stock.

**Risks Related to Legal and Compliance Matters**

***We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability and have to limit the commercialization of any approved products and/or our product candidates.***

The use of our product candidates in clinical trials, and the sale of any product for which we obtain regulatory approval, exposes us to the risk of product liability claims. We face inherent risk of product liability related to the testing of our product candidates in human clinical trials, including liability relating to the actions and negligence of our investigators, and will face an even greater risk if we commercially sell any product candidates that we may develop. For example, we may be sued if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. Product liability claims might be brought against us by consumers, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of merit or eventual outcome, liability claims may result in:

- loss of revenue from decreased demand for our products and/or product candidates;
- impairment of our business reputation or financial stability;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- diversion of management attention;
- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs;
- the inability to commercialize our product candidates;
- significant negative media attention;
- decreases in our stock price;
- initiation of investigations and enforcement actions by regulators; and
- product recalls, withdrawals or labeling, marketing or promotional restrictions, including withdrawal of marketing approval.

We believe we have sufficient insurance coverage in place for our business operations. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain FDA or comparable foreign regulatory approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing, or at all. Failure to obtain and retain

sufficient product liability insurance at an acceptable cost could prevent or inhibit the commercialization of products we develop. On occasion, large judgments have been awarded in class action lawsuits based on therapeutics that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash, and materially harm our business, financial condition, results of operations, stock price and prospects.

***We are subject to the U.S. Foreign Corrupt Practices Act and other anti-corruption laws, as well as import and 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, financial condition, results of operations, stock price and prospects.***

Our operations are subject to anti-corruption laws, including the Foreign Corrupt Practices Act (FCPA), and other anti-corruption laws that apply in countries where we do business. The FCPA and these other laws generally prohibit us 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 also may participate in collaborations and relationships with third parties whose actions, if non-compliant, could potentially subject us to liability under the FCPA 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 government of the United States, including applicable import and export control regulations, economic sanctions on countries and persons, anti-money laundering laws, customs requirements and currency exchange regulations, collectively referred to as the trade control laws.

We can provide no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws or other legal requirements, including trade control laws. If we are not in compliance with applicable 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 an adverse impact on our business, financial condition, results of operations, stock price and prospects. Likewise, any investigation of any potential violations of these anti-corruption laws or trade control laws by United States or other authorities could also have an adverse impact on our reputation, our business, financial condition, results of operations, stock price and prospects.

***If we fail to comply with federal and state healthcare laws, including fraud and abuse and health and other information privacy and security laws, we could face substantial penalties and our business, financial condition, results of operations, stock price and prospects will be materially harmed.***

We are subject to many federal and state healthcare laws, such as the federal Anti-Kickback Statute, the federal civil and criminal False Claims Acts, the civil monetary penalties statute, the Medicaid Drug Rebate statute and other price reporting requirements, the Veterans Health Care Act of 1992 (VHCA), HIPAA, the FCPA, the ACA and similar state laws. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws, and regulations pertaining to fraud and abuse, reimbursement programs, government procurement, and patients' rights are and will be applicable to our business. We would be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states and foreign jurisdictions in which we conduct our business. In the European Union, the data privacy laws are generally stricter than those which apply in the United States and include specific requirements for the collection of personal data of European Union persons or the transfer of personal data outside of the European Union to the United States to ensure that European Union standards of data privacy will be applied to such data. For more information, see Part I, Item 1 "Business – Other Healthcare Laws and Compliance Requirements."

If we or our operations, including our arrangements with physicians and other healthcare providers, some of whom receive share options or other financial interest in the business as compensation for services provided, are found to be in violation of any federal or state healthcare law, or any other governmental laws or regulations that apply to us, we may be subject to penalties, including civil, criminal, and administrative penalties, damages, fines, disgorgement, suspension and debarment from government contracts, and refusal of orders under existing government contracts, exclusion from participation in U.S. federal or state health care programs, corporate integrity agreements, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it or they may be subject to criminal, civil or administrative sanctions, including but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal,

state and foreign privacy, data protection, security, reimbursement, and fraud laws may prove costly. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

***Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.***

Changes in tax law may adversely affect our business or financial condition. Any new taxes could adversely affect our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, under Section 174 of the Internal Revenue Code of 1986, as amended (the Code), in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the U.S. will be capitalized and amortized, which may have an adverse effect on our cash flow. In addition, it is uncertain if and to what extent various states will conform to changes to U.S. federal income tax law. We urge prospective investors in our common stock to consult with their legal and tax advisors with respect to any recently enacted tax legislation, or proposed changes in law, and the potential tax consequences of investing in or holding our common stock.

***Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.***

Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership by 5% stockholders over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income may be limited. As a result of our most recent private placements, the IPO, and other transactions that have occurred over the past three years, we may have experienced, an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2022, we had U.S. federal and state net operating loss carryforwards of $65.9 million and $61.9 million, which begin to expire in 2027 and 2032, respectively, and which could be limited if we experience an "ownership change." The reduction of the corporate tax rate under TCJA may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Under current federal tax law, federal net operating losses generated after December 31, 2017 will not be subject to expiration but will not be permitted to be carried back. In addition, under current U.S. federal tax law, the amount of net operating losses generated after December 31, 2020 that we are permitted to deduct in any taxable year is limited to 80% of our taxable income in such year, where taxable income is determined without regard to the net operating loss deduction itself. Additionally, as of December 31, 2022, we had a U.S. federal net operating loss carryforward of $57.1 million which do not expire but is limited to an annual deduction equal to 80% of annual taxable income.

***If third-party payors fail to provide adequate coverage, reimbursement and payment rates for our product candidates, or if health maintenance organizations or long-term care facilities choose to use therapies that are less expensive or considered a better value, our revenue and prospects for profitability will be limited.***

In both domestic and foreign markets, sales of our products will depend in part upon the availability of coverage and reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers, and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new therapeutic products when more established or lower cost therapeutic alternatives are already available or subsequently become available, even if our products are alone in a class. If reimbursement is not available, or is available only to limited levels, our product candidates may be competitively disadvantaged, and we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain

a market share sufficient to realize a sufficient return on our or their investments. Alternatively, securing favorable reimbursement terms may require us to compromise pricing and prevent us from realizing an adequate margin over cost. For more information, see Part I, Item 1 "Business - Coverage and Reimbursement."

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved therapeutics. Marketing approvals, pricing, and reimbursement for new therapeutic 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 therapeutic before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription biopharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval. Our ability to commercialize our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Regulatory authorities and third-party payors, such as private health insurers, and health maintenance organizations, decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Several third-party payors are requiring that companies provide them with predetermined discounts from list prices, are using preferred drug lists to leverage greater discounts in competitive classes, are disregarding therapeutic differentiators within classes, are challenging the prices charged for therapeutics, and are negotiating price concessions based on performance goals.

Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. If payors subject our product candidates to maximum payment amounts, or impose limitations that make it difficult to obtain reimbursement, providers may choose to use therapies which are less expensive when compared to our product candidates. Additionally, if payors require high copayments, beneficiaries may seek alternative therapies. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any products to the satisfaction of hospitals, other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

In addition, federal programs impose penalties on manufacturers of therapeutics in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. A few states have also passed or are considering legislation intended to prevent significant price increases. Regulatory authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease, discount, or rebate a portion of the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the realized prices for our products, if any, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

In addition, third-party payors are increasingly requiring higher levels of evidence of the benefits and clinical outcomes of new technologies, benchmarking against other therapies, seeking performance-based discounts, and challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

***We are subject to new legislation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance, and adversely affect our ability to market our products, obtain collaborators and raise capital.***

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 prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval. We expect that 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 may receive for any approved products. For more information, see Part I, Item 1 "Business - Health Reform."

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

***Our employees, independent contractors, consultants, commercial partners, principal investigators, CROs or CMOs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could have a material adverse effect on our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, independent contractors, consultants, commercial partners, principal investigators, CMOs or CROs could include intentional, reckless, negligent, or unintentional failures to comply with FDA regulations, comply with applicable fraud and abuse laws, provide accurate information to the FDA, properly calculate pricing information required by federal programs, report financial information or data accurately or disclose unauthorized activities to us. This misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter this type of misconduct, 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 or regulations. Moreover, it is possible for a whistleblower to pursue a False Claims Act case against us even if the government considers the claim unmeritorious and declines to intervene, which could require us to incur costs defending against such a claim. 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, financial condition, results of operations, stock price and prospects, including the imposition of significant fines or other sanctions.

***Violations of or liabilities under environmental, health and safety laws and regulations could subject us to fines, penalties or other costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures, the handling, use, storage, treatment and disposal of hazardous materials and wastes and the cleanup of contaminated sites. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We would incur substantial costs as a result of violations of or liabilities under environmental requirements in connection with our

operations or property, including fines, penalties and other sanctions, investigation and cleanup costs and third-party claims. Although we generally contract with third parties for the disposal of hazardous materials and wastes from our operations, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, 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 connection with our storage or disposal of biological, hazardous or radioactive materials.

**Risks Related to Our Reliance on Third Parties**

***For certain product candidates, we depend, or will depend, on development and commercialization collaborators to develop and conduct clinical trials with, obtain regulatory approvals for, and if approved, market and sell product candidates. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed.***

For certain product candidates, we depend, or will depend, on our development and commercial collaborators to develop, conduct clinical trials of, and, if approved, commercialize product candidates. We cannot provide assurance that our collaborators will be successful in or that they will devote sufficient resources to these collaborations. If our current or future collaboration and commercialization partners do not perform in the manner we expect or fail to fulfill their responsibilities in a timely manner, or at all, if our agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to their and our product candidates and products could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such product candidates. Moreover, our ability to generate revenues from these collaborations and product candidates will depend on such collaborators' abilities to perform in the manner we expect or fulfill their responsibilities in a timely manner, and delays by collaborators, or caused by other collaboration contract obligations, may result in a delay of our ability to disclose data.

Our current collaborations and any future collaborations that we enter into are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to the collaborations;
- collaborators may not perform their obligations as expected or fail to fulfill their responsibilities in a timely manner, or at all;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay preclinical studies or clinical trials, provide insufficient funding for clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could fail to make timely regulatory submissions for a product candidate;
- 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- the collaborations may not result in product candidates to develop and/or preclinical studies or clinical trials conducted as part of the collaborations may not be successful;
- product candidates developed with collaborators may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to stop commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate; and
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.

In addition, certain collaboration and commercialization agreements provide our collaborators with rights to terminate such agreements, which rights may or may not be subject to conditions, and which rights, if exercised, would adversely affect our product development efforts and could make it difficult for us to attract new collaborators. For example, our license agreement with MGB may be terminated by MGB for our failure to pay, our failure to maintain proper insurance in accordance with the agreement, if we file for bankruptcy or if we remain in default for non-financial reasons following a specified cure period to remedy the breach. In the event of the termination of any collaboration or commercialization agreement, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidates or products; we would likely be required to seek additional financing to fund further development or identify alternative strategic collaborations; our potential to generate future revenue from royalties and milestone payments from such product candidates or products would be significantly reduced, delayed or eliminated; and it could have an adverse effect on our business and future growth prospects. Our rights to recover tangible and intangible assets and intellectual property rights needed to advance a product candidate or product after termination of a collaboration may be limited by contract, and we may not be able to advance a program post-termination.

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation in the business and financial communities could be adversely affected. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations and prospects.

***If conflicts arise with our development and commercialization collaborators or licensors, they may act in their own self-interest, which may be adverse to the interests of our company.***

We may in the future experience disagreements with our development and commercialization collaborators or licensors. Conflicts may arise in our collaboration and license arrangements with third parties due to one or more of the following:

- disputes with respect to milestone, royalty and other payments that are believed due under the applicable agreements;
- disagreements with respect to the ownership of intellectual property rights or scope of licenses;
- disagreements with respect to the scope of any reporting obligations;
- disagreements with respect to contract interpretation or the preferred course of development;
- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities; and
- disputes with respect to a collaborator's or our development or commercialization efforts with respect to our products and product candidates.

Conflicts with our development and commercialization collaborators or licensors could materially adversely affect our business, financial condition or results of operations and future growth prospects.

***We rely on third parties, including independent clinical investigators and CROs to conduct and sponsor some of the clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.***

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, academic partners, medical institutions, regulatory affairs consultants and third-party CROs, to conduct our preclinical studies and clinical trials, including in some instances sponsoring such clinical trials, and to engage with regulatory authorities and monitor and manage data for our ongoing preclinical and clinical programs. While we have, or will have, agreements governing the activities of such third parties, we will control only certain aspects of their activities and have limited influence over their actual performance.

Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

We remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the EEA and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our academic partners or CROs or if we or any of our academic partners or CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us, our academic partners or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, 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 may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, with respect to investigator-sponsored trials that are being or may be conducted, we do not control the design or conduct of these trials, and it is possible that the FDA or EMA will not view these investigator-sponsored trials as providing adequate support for future clinical trials or market approval, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. We expect that such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including the ability to obtain a license to obtain access to use and reference the data, including for our own regulatory submissions, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. Additionally, the FDA or EMA may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or EMA may require us to obtain and submit additional preclinical, manufacturing, or clinical data.

***If the manufacturers upon which we may rely fail to produce our product candidates in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to biopharmaceutical manufacturers, we may face delays in the development and commercialization of, or be unable to meet demand for, our product candidates and may lose potential revenues.***

We also expect to develop commercial-scale manufacturing at third-party manufacturers for our product candidate CAN-2409. We may develop clinical manufacturing capabilities at our facility in Needham, Massachusetts for our product candidate CAN-3110 and we may also develop clinical-scale manufacturing for CAN-3110 at third-party manufacturers. There can be no assurance that our supply of clinical product will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified replacements. Any delays in

obtaining adequate supplies of our product candidates that meet the necessary quality standards, including delays caused by the COVID-19 pandemic, may delay our development or commercialization.

We may not succeed in our efforts to establish manufacturing relationships or other alternative arrangements for any of our product candidates or programs. Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing and filling our viral product for us and willing to do so. If our existing third-party manufacturers, or the third parties that we engage in the future, should cease to work with us, we likely would experience delays in obtaining sufficient quantities of our product candidates for us to meet commercial demand or to advance our clinical trials while we identify and qualify replacement suppliers. If for any reason we are unable to obtain adequate supplies of our product candidates or the therapeutic substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively. Further, even if we do establish such collaborations or arrangements, our third-party manufacturers may breach, terminate, or not renew these agreements.

Any problems or delays we experience in preparing for commercial-scale manufacturing of a product candidate or component may result in a delay in product development timelines and FDA or comparable foreign regulatory authority approval of the product candidate or may impair our ability to manufacture commercial quantities or such quantities at an acceptable cost and quality, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates and may materially harm our business, financial condition, results of operations, stock price and prospects.

The manufacture of biopharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of therapeutics often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel or key raw materials, and compliance with strictly enforced federal, state, and foreign regulations. Our CMOs may not perform as agreed. If our manufacturers were to encounter these or other difficulties, our ability to provide product candidates to patients in our clinical trials could be jeopardized.

CMOs of our product candidates may be unable to comply with our specifications, applicable cGMP requirements or other FDA, state or foreign regulatory requirements. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. Any such deviations may also require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business. Any delays in obtaining products or product candidates that comply with the applicable regulatory requirements may result in delays to clinical trials, product approvals, and commercialization. It may also require that we conduct additional studies.

While we are ultimately responsible for the manufacturing of our product candidates and therapeutic substances, other than through our contractual arrangements, we have little control over our manufacturers' compliance with these regulations and standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any new manufacturers would need to either obtain or develop the necessary manufacturing know-how, and obtain the necessary equipment and materials, which may take substantial time and investment. We must also receive approval from the FDA and applicable comparable foreign regulatory authorities for the use of any new manufacturers for commercial supply. The regulatory authorities may also require additional studies if a new manufacturer is relied upon for commercial production. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product or product candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or once approved, to commercialize those product candidates in a timely manner or within budget. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies, which could require the conduct of additional

clinical trials. Accordingly, switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

A failure to comply with the applicable regulatory requirements, including periodic regulatory inspections, may result in regulatory enforcement actions against our manufacturers or us (including fines and civil and criminal penalties, including imprisonment) suspension or restrictions of production, injunctions, delay or denial of product approval or supplements to approved products, clinical holds or termination of clinical trials, warning or untitled letters, regulatory authority communications warning the public about safety issues with the product candidate, refusal to permit the import or export of the products, product seizure, detention, or recall, operating restrictions, suits under the civil False Claims Act, corporate integrity agreements, consent decrees, withdrawal of product approval, environmental or safety incidents and other liabilities. If the safety of any quantities supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

Any failure or refusal to supply our product candidates or components for our product candidates that we may develop could delay, prevent or impair our clinical development or commercialization efforts. Any change in our manufacturers could be costly because the commercial terms of any new arrangement could be less favorable and because the expenses relating to the transfer of necessary technology and processes could be significant.

***Some of our product candidates are being and may be studied in third-party research and clinical trials sponsored by organizations or agencies other than us, or in investigator-sponsored clinical trials, which means we will have minimal or no control over the conduct of such trials and which may adversely affect our ability to obtain marketing approval or certain regulatory exclusivities.***

We have supplied and may continue to supply and otherwise support third party research, including investigator-sponsored clinical trials. Investigator-sponsored clinical trials pose similar risks as those set forth elsewhere in this "Risk Factors" section relating to our internally-sponsored clinical trials, but because we are not be the sponsors of these trials, we have less control over the protocols, administration or conduct of these trials, including follow-up with patients and ongoing collection of data after treatment. Additionally, third party clinical research has been and may continue to be conducted with CAN-3110 and CAN-2409 which was not provided by us. The conduct or findings of these trials may have a negative impact on our development programs notwithstanding that we have little involvement or control over these trials. As a result, we are subject to additional risks associated with the way investigator-sponsored trials are conducted. In particular, for trials in which we supply drug product, we may be named in lawsuits that would lead to increased costs associated with legal defense. Additional risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues and difficulties or differences in interpreting data. Third-party investigators may design clinical trials with clinical endpoints that are more difficult to achieve, or in other ways that increase the risk of negative clinical trial results compared to clinical trials that we may design on our own. Negative results in investigator-sponsored clinical trials could have a material adverse effect on our efforts to obtain regulatory approval for our product candidates and the public perception of our product candidates. As a result, our lack of control over the conduct and timing of and communications with the FDA and other regulatory authorities regarding investigator-sponsored trials may expose us to additional risks and uncertainties, many of which are outside our control, and the occurrence of which could adversely affect the commercial prospects for our product candidates. In addition, third parties that are investigating product candidates which have not been provided by us may seek and obtain regulatory approval of product candidates before we do, which may adversely affect our development strategy and eligibility for certain exclusivities for which we may otherwise be eligible.

***We have completed and may in the future complete related party transactions that were not and may not be conducted on an arm's length basis.***

We have in the past been and continue to be party to certain transactions with certain entities affiliated with Estuardo Aguilar-Cordova, our founder and former Chief Scientific Officer, and Laura Aguilar, our former Chief Medical Officer. For instance, we have entered into an exclusive license agreement with Ventagen, LLC (Ventagen), an entity owned in part (49.5%), though not managed, by Estuardo Aguilar-Cordova and Laura Aguilar, for the use of worldwide patent rights and know-how owned or controlled by us which cover applicable technology utilizing the delivery method of the herpes derived TK protein to tumors or other tissues via a viral vector.

In January 2008, we entered into an operating lease agreement with a term through December 31, 2022 with Ellka Holdings, LLC (Ellka), for the space in which we operated in Auburndale, MA. In May 2016, we entered into a second lease agreement with Ellka for living space for employees, also in Auburndale, MA. We entered into a second lease for this space on July 26, 2018, which expired on July 31, 2019. Ellka was originally established in 2007 as an LLC for the purpose of acquiring and managing investment properties owned by Laura Aguilar and Estuardo Aguilar-Cordova and their children's trusts. Ellka is owned and operated by Laura Aguilar and Estuardo Aguilar-Cordova and members of their immediate family. Although we believe that these transactions were conducted on an arm's length basis, it is possible that the terms were less favorable to us than they might have been in a transaction with an unrelated party.

As of March 15, 2023, Estuardo Aguilar-Cordova and Laura Aguilar beneficially owned 6,216,971 shares of our common stock, or approximately 21.5% of our total outstanding capital stock as of such date. Accordingly, they will continue to have significant influence over all business decisions, including with respect to such matters as amendments to our charter, other fundamental corporate transactions, such as mergers, asset sales, and the sale of the Company, and otherwise will be able to influence our business and affairs. In connection with the IPO, we adopted a written related-person transactions policy that sets forth our policies and procedures regarding the identification, review, consideration and oversight of related-person transactions.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to manufacture our product candidates, and because we collaborate with various organizations and academic institutions on the development of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets.

Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

**Risks Related to Intellectual Property**

***Our rights to develop and commercialize certain of our product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.***

We are and expect to continue to be reliant upon third-party licensors for certain patent and other intellectual property rights that are important or necessary to the development of some of our technology and product candidates. For example, we rely on licenses from MGB and Periphagen to certain patent rights. These license agreements impose, and we expect that any future license agreement will impose, specified diligence, milestone payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses.

Furthermore, our licensors have, or may in the future have, the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. For example, Periphagen has asserted that we have failed to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset as required in our exclusive license agreement with Periphagen. Periphagen has triggered the dispute and escalation provisions under the Periphagen License Agreement. If we are unable to resolve the issue and an arbitrator concludes that we failed to use such commercially reasonable efforts, then we may submit a specified payment in lieu of satisfying such obligations or Periphagen may terminate the Periphagen License Agreement. If our Periphagen license or our other license agreements are terminated, we may lose our rights to develop and commercialize certain of our product candidates and technology, lose patent protection, experience significant delays in the development and commercialization of certain of our product candidates and technology, and incur liability for damages. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors

or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with any product candidates we may develop and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other 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 current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, our license agreements are, and future license agreements are likely to be, 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 diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

License agreements we may enter into in the future may be non-exclusive. Accordingly, third parties may also obtain non-exclusive licenses from such licensors with respect to the intellectual property licensed to us under such license agreements. Accordingly, these license agreements may not provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and any product candidates we may develop in the future.

Moreover, some of our in-licensed patent and other intellectual property rights may in the future be subject to third-party interests such as co-ownership. If we are unable to obtain an exclusive license to such third-party co-owners' interest, in such patent and other intellectual property rights, such third-party co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. We or our licensors may need the cooperation of any such co-owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors.

Additionally, we may not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. It is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our technology and any product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products.

Furthermore, our owned and in-licensed patent rights may be subject to a reservation of rights by one or more third parties. When new technologies are developed with government funding, in order to secure ownership of patent rights

related to the technologies, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U.S. government and timely electing title to such inventions. A failure to meet these obligations may lead to a loss of rights or the unenforceability of relevant patents or patent applications.

***Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.***

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. 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 may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications and patents we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology and directed to our product candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our product candidates.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and patents, and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications and patents. Similarly, for United States applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor's disclosure.

We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor's technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that may issue that cover our 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 the patents we in-license or narrow the scope of our patent protection. In addition, the laws of

foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law is more restrictive than U.S. patent law in connection with the patentability of methods of treatment of the human body and Chinese bankruptcy law may not provide a licensee the same protections as U.S. bankruptcy law.

Furthermore, in the United States, patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the Leahy-Smith America Invents Act (the America Invents Act), enacted in 2013, the United States moved from a “first to invent” to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are unclear as the USPTO continues to develop new regulations and procedures in connection with the America Invents Act. In addition, the patent positions of companies in the development and commercialization of biopharmaceuticals 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 increase the uncertainties and costs surrounding the prosecution of our patent applications and have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

In addition, a European Unified Patent Court (UPC) is scheduled to come into force during 2023. The UPC will be a common patent court to hear patent infringement and revocation proceedings effective for member states of the European Union. This could enable third parties to seek revocation of any of our European patents in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. Any such revocation and loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce or defend the validity of our European patents. We may decide to opt out our European patents and patent applications from the UPC. If certain formalities and requirements are not met, however, our European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC.

We cannot predict whether the patent applications we in-license currently being pursued will issue as patents, whether the claims of any patent that has or may issue will provide us with a competitive advantage or prevent competitors from designing around the claims to develop competing technologies in a non-infringing manner, or whether we or our licensors will be able to successfully pursue patent applications in the future relating to our current product candidates or future products and product candidates. Moreover, the patent application and approval process is expensive and time-consuming. We or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Furthermore, we, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to seek additional patent protection.

Even if the patent applications we in-license 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. Our competitors may be able to circumvent our patent rights by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our product candidates. Alternatively, our competitors may seek to market generic versions of any approved products by submitting abbreviated BLAs to the FDA during which process they may claim that patents licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our intellectual property rights, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find the patents we in-license invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have in-licensed valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents or those of our licensors;

- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned, co-owned, or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned, co-owned, or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- the co-owners of certain of our patent applications may become involved with, or license or assign the co-owned applications to competitors , or become hostile to us or the patents or patent applications on which they are named as co-owners;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

***We may enter into license or other collaboration agreements in the future that may impose certain obligations on* us. If we fail to comply with our obligations under such future agreements with third parties, we could lose license rights that may be important to our future business.**

In connection with our efforts to expand our pipeline of product candidates, we may enter into certain licenses or other collaboration agreements in the future pertaining to the in-license of rights to additional candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

Moreover, 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 product candidates, 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 priority of invention of patented 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 product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In addition, we may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

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

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. For example, our clinical development strategy includes the testing of live tissue samples, and our techniques for preserving and testing these samples are proprietary and confidential. If one or more third parties obtain or are otherwise able to replicate these techniques, an important feature and differentiator of our clinical development strategy will become available to potential competitors. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

***Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.***

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post-grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. 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 developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

***Our collaborators may assert ownership or commercial rights to inventions they develop from research we support or that we develop from our use of the tissue samples or other biological materials, which they provide to us, or otherwise arising from the collaboration.***

We collaborate with several institutions, universities, medical centers, physicians and researchers in scientific matters and expect to continue to enter into additional collaboration agreements. In certain cases, we do not have written agreements with these collaborators, or the written agreements we have do not cover intellectual property rights. Also, we rely on numerous third parties to provide us with tissue samples and biological materials that we use to conduct our research activities and develop our product candidates. If we cannot successfully negotiate sufficient ownership and commercial rights to any inventions that result from our use of a third-party collaborator's materials, or if disputes arise with respect to the intellectual property developed with the use of a collaborator's samples, or data developed in a collaborator's study, we may be limited in our ability to capitalize on the market potential of these inventions or developments.

***Third parties may assert that we are employing their proprietary technology without authorization.***

There may be third-party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of

our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. 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, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

***Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information, misappropriated trade secrets, or are in breach of non-competition or non-solicitation agreements with our competitors.***

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. We may also be subject to claims that we caused an employee to breach the terms of their non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor or other party. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, 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. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources.

Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

***We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.***

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. We may develop products containing our compounds and pre-existing biopharmaceutical compounds. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual

property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, 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 size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will 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.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.***

Competitors may infringe our patents or the patents of our current or future licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. 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.

We may choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an ex-parte re-examination, inter partes review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third-party's patent in patent opposition proceedings in the European Patent Office (EPO), or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference or derivation proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

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 or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it 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. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could 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 substantial adverse effect on the price of our common stock.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

***Any patents, if issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.***

If we or one of our licensors initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Likewise, we own a U.S. patent relating to our CAN-2409 product candidate that expires in 2034, and our in-licensed U.S. and non-U.S. patents relating to our HSV-based product candidates, licensed from MGB and from Periphagen are expected to expire in 2036 and in 2037, respectively, without taking into account any possible patent term extensions. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. We own and in-license pending patent applications relating to our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2034 through 2042, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

***We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.***

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. 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. 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 but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims 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, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent 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 or interpreted narrowly and 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Patent terms may be inadequate to protect our competitive position on our 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 such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension 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 applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

***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.***

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. 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.

**Risks Related to Our Common Stock**

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses to stockholders.***

Our stock price is likely to continue to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance

of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which it was purchased. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- commencement or termination of collaboration, licensing or similar arrangements for our development programs;
- announcements by our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- developments or setbacks related to drugs that are co-administered with any of our product candidates, such as checkpoint inhibitors;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- expiration of market stand-off or lock-up agreements;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions and overall fluctuations in the financial markets in the United States and abroad; and
- the other factors described in this “Risk Factors” section.

In addition, the trading prices for our and other biopharmaceutical companies’ stock have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock and any such sales may be on unfavorable terms. The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak further impacts our business, including our preclinical studies and clinical trials, results of operations and financial condition will depend on future developments which are highly uncertain and cannot be predicted with confidence. Such factors include, but are not limited to, the duration of the outbreak, the impact of variants, travel restrictions, quarantines, shelter-in-place orders and social distancing, business closures or business disruptions, the adoption and effectiveness of vaccines and vaccine distribution efforts, and the effectiveness of other actions taken in the United States and other countries to contain and treat the disease.

***Raising additional capital through the sale of a substantial number of shares of our common stock, or the perception that sales of a substantial number of shares of our common stock might occur, may cause dilution to our stockholders, could cause our stock price to decline and could restrict our operations or require us to relinquish rights to our technologies or current or future product candidates.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that may materially adversely affect your rights as a common stockholder. In August 2022, we filed a registration statement on Form S-3 (Shelf) pursuant to which we may issue up to $75.0 million in shares of common stock in sales deemed to be “at-the-market offerings” (the ATM Program) as defined by the Securities Act of 1933, as amended (Securities Act), and up to $200.0 million in shares of our common stock, preferred stock, debt securities, warrants and/or units. Any sale or issuance of securities pursuant to this registration statement or otherwise may result in dilution to our stockholders and may cause our stock price to decline. Due to the SEC’s “baby shelf rules,” which prohibit companies with a public float of less than $75.0 million from issuing securities under a shelf registration

statement in excess of one third of such company's public float in a 12-month period, we are currently only able to issue a limited number of shares which aggregate to no more than one-third of our public float using our Shelf. Although alternative public and private transaction structures may be available, these may require additional time and cost, may impose operational restrictions on us, and may not be available on attractive terms.

Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, acquiring, selling or licensing intellectual property rights, making capital expenditures, declaring dividends, or other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to meet certain milestones in connection with debt financing and the failure to achieve such milestones by certain dates may force us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us which could have a material adverse effect on our business, operating results and prospects.

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, research programs or current or future product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, scale back or discontinue the development and commercialization of one or more of our product candidates, delay our pursuit of potential in-licenses or acquisitions or grant rights to develop and market current or future product candidates that we would otherwise prefer to develop and market ourselves.

***We are an "emerging growth company" as defined in the JOBS Act and a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended (the Exchange Act), and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.***

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.235 billion or more; (ii) December 26, 2026; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the SOX Act (Section 404);
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, we have provided only two years of audited financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure, and we have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we no longer qualify an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter.

Although we are still evaluating the JOBS Act, we currently intend to take advantage of some, but not all, of the reduced regulatory and reporting requirements that will be available to us so long as we qualify as an “emerging growth company” and “smaller reporting company.” We have elected to avail ourselves of this exemption and, therefore, we are not subject to the same new or revised accounting standards as other public companies that are not emerging growth companies or smaller reporting company. As a result, changes in rules of U.S. GAAP or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an “emerging growth company,” which may increase the risk that material weaknesses or significant deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as a “smaller reporting company” or an “emerging growth company,” we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

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

As a public company, and particularly after we are no longer an “emerging growth company,” we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the SOX Act and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the Dodd-Frank Act), was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as “say on pay” and proxy access. Emerging growth companies may implement many of these requirements over a longer period and up to five years from the pricing of an initial public offering. We intend to take advantage of these extended transition periods but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to maintain director and officer liability insurance. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard,

we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In additional, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

***Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.***

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of March 15, 2023, we had a total of 28,919,810 shares of common stock outstanding.

In addition, shares of common stock that are reserved for future issuance under our 2021 Plan and our 2021 Employee Stock Purchase Plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of 8,884,661 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in such shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

***Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.***

The existing holdings of our executive officers, directors, principal stockholders and their affiliates represent beneficial ownership, in the aggregate, of approximately 59.9% of our outstanding common stock with Estuardo Aguilar-Cordova and Laura Aguilar (together, both directly and indirectly) beneficially owning approximately 21.5% of our outstanding common stock, and with entities and persons affiliated with PBM Capital Group, LLC (PBM Capital), beneficially owning approximately 29.4% of our outstanding common stock. In addition, Diem Nguyen, who is a member of our Board of Directors, is currently Chief Executive Officer of Xalud Therapeutics, Inc., which is majority-owned by PBM Capital. As a result, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

***Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;

- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

***Our bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.***

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware Forum Provision. The Delaware Forum Provision does not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as our principal office is located in Needham, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an

action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***We may be subject to securities litigation, which is expensive and could divert management's attention.***

The market price of our common stock may be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In particular, the trading prices for pharmaceutical, biopharmaceutical and biotechnology companies have been highly volatile as a result of the COVID-19 pandemic. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management’s attention from other business concerns, which could seriously harm our business.

***The number of shares of our common stock outstanding may increase substantially as a result of our November 2018 issuance of warrants to purchase up to an aggregate of 7,344,968 shares of common stock.***

In connection with the November 13, 2018 issuance of Series B convertible preferred stock (the Series B Preferred), we issued to the purchaser of the Series B Preferred, warrants to purchase 3,672,484 shares of common stock for $6.81 per share (the Series B Warrants) which were and remain fully exercisable upon issuance. The Series B Warrants contain provisions allowing cashless exercise.

In addition, we issued to the same stockholder additional five-year warrants for the purchase of 3,672,484 shares of common stock for $6.81 per share (the Conditional Series B Warrants), which become exercisable in the event that we complete a future financing that meets certain financial milestones or achieves certain share prices as follows:

- 918,121 shares vest upon (1) a financing event effected through the sale of our equity securities to third parties resulting in at least $20,000,000 in gross proceeds with a per share price of $12.47, or (2) an average market price (determined over a consecutive 10-day period) of $12.47 per share;
- an additional 918,121 shares vest upon (1) a financing event with a price per share of $13.20, or (2) an average market price (determined over a consecutive 10-day period) of, $13.20 per share;
- an additional 918,121 shares vest upon (1) a financing event with a per share price of $13.94, or (2) an average market price (determined over a consecutive 10-day period) of, $13.94 per share; and
- an additional 918,121 shares vest upon (1) a financing event with a per share price of $14.68, or (2) an average market price (determined over a consecutive 10-day period) of, $14.68 per share.

On June 24, 2021, our board of directors approved, and on July 14, 2021, our stockholders approved, effective upon the closing of the IPO, an amendment to the terms of the Series B Warrants and the Conditional Series B Warrants to extend the expiration date from November 2023 to November 2025. In addition, the exercise period for the Conditional Series B Warrants was amended such that in the event the future financing milestones or certain share price targets described above are achieved, the Conditional Series B Warrants can only be exercised in conjunction with the sale of the company, on a cash or cashless exercise basis, or otherwise in November 2025 through a cashless exercise.

We recorded the Series B Warrants as a component of stockholder’s equity at the time of issuance at their estimated fair value of $2.1 million and recorded the Conditional Series B Warrants as a liability on the consolidated balance sheet because the number of shares used to calculate the settlement is not a fixed number of shares. The Conditional Series B Warrants are remeasured to their fair value at each reporting date with changes in the fair value recognized as a component of other income (expense), net in the consolidated statements of operations. We will continue to recognize changes in the fair value of the Conditional Series B Warrants until each Conditional Series B Warrant is exercised, expires or qualifies for equity classification.

The exercise of these warrants in full, assuming vesting in full of the Conditional Series B Warrants and no net exercise, would result in an additional 7,344,968 shares of common stock outstanding, resulting in substantial dilution to stockholders who hold our common stock. In addition, if the holders of these warrants, including PBM Capital, were to

exercise such warrants in full, these holders could then have significant influence over the outcome of any stockholder vote, including the election of directors and the approval of mergers or other business combination transactions.

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

None.

**Item 2. Properties.**

Our principal office is located at 117 Kendrick St, Suite 450, Needham, Massachusetts 02494, where we lease approximately 15,000 square feet of office and laboratory space. We lease this space under a lease that terminates on August 31, 2026.

**Item 3. Legal Proceedings.**

From time to time, we may become involved in litigation or other legal proceedings. On December 15, 2022, Periphagen notified us by letter of its claim that we have failed to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset under an Exclusive License Agreement dated December 9, 2019 between us and Periphagen (the "Periphagen License Agreement"). We have denied Periphagen's claims. On January 13, 2023, we filed a demand for arbitration against Periphagen with the American Arbitration Association, seeking a declaration that Periphagen's December 15 letter failed to comply with the dispute and escalation provisions in the Periphagen License Agreement. After filing the demand, the parties began engaging in the dispute and escalation process under the Periphagen License Agreement. On March 10, 2023, Periphagen filed its answer and counterclaims to our demand for arbitration. In its counterclaims, Periphagen seeks a declaration that we have not used commercially reasonable efforts to complete a human proof of concept clinical trial of the NT-3 Asset and a declaration that any further extension of time would not be scientifically or commercially reasonable. Periphagen also seeks a declaration that we must use commercially reasonable efforts to develop the NT-3 Asset during any remaining time under the agreement. We have denied Periphagen's counter claims.

In the event the parties are unable to resolve the dispute as part of the escalation process, an arbitrator will decide whether we have used commercially reasonable efforts. In the event that the arbitrator determines that we have not used commercially reasonable efforts, then we may submit a specified payment in lieu of satisfying such obligations.

Aside from the proceeding with Periphagen, we are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

**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 Securities.

**Market Information**

Our common stock is traded under the symbol "CADL" on the Nasdaq Global Market and has been publicly traded since July 27, 2021. Prior to this time, there was no public market for our common stock.

On March 15, 2023, there were approximately 131 registered holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Dividend Policy**

We have never declared or paid any dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

**Unregistered Sales of Equity Securities and Use of Proceeds**

***Recent Sales of Unregistered Equity Securities***

None.

***Use of Proceeds***

The offer and sale of all the shares of our common stock in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (Reg. No. 333-257444), as amended, which was declared effective by the SEC on July 26, 2021. There has been no material change in the expected use of the net proceeds from our Annual Report on Form 10-K for the year ended December 31, 2021 as filed with the SEC on March 29, 2022.

***Purchases of Equity Securities by the Issuer and Affiliated Purchasers***

None.

**Item 6. Reserved.**

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis contains forward-looking statements that involve risks and uncertainties. You should review the section titled "Risk factors" in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described below.

**Overview**

We are a clinical stage biopharmaceutical company focused on developing and commercializing viral immunotherapies to help patients fight cancer. Our engineered viruses are designed to induce a systemic anti-tumor response due to immunogenic cell death through direct viral-mediated cytotoxicity in cancer cells, thus releasing tumor neo-antigens and creating a pro-inflammatory microenvironment. Our viral immunotherapy approach utilizes intratumoral administration of genetically engineered viruses to induce tumor cell death and elicit a systemic anti-tumor response. Local delivery enables us to achieve these effects while aiming to minimize systemic toxicity. The immune cells induced by these viral immunotherapies are believed to target patients' specific tumor antigens, potentially improving responses in immunologically "hot" tumors while at the same time infiltrating the tumor microenvironment, transforming non-inflamed "cold" tumors with limited immune response into "hot" tumors. While our product candidates are administered directly into the tumor, we have observed systemic immune response in our preclinical studies and clinical trials that may indicate the potential of our product candidates to induce systemic immune response against distal, uninjected tumors, also known as an "abscopal" effect.

We believe viral immunotherapy is among the most promising cancer treatment modalities today. Our goal is to further improve patient outcomes through viral immunotherapies by selecting the optimal vector, specific transgenes and clinical indications for each tumor type while optimizing product candidate attributes, such as high-titer formulation, intratumoral administration to induce systemic anti-tumor immunity, and storage conditions that could potentially lower logistical barriers for patients and clinicians.

We have established two clinical stage viral immunotherapy platforms based on novel, genetically modified adenovirus and herpes simplex virus (HSV) constructs, respectively.

Our most advanced product candidate, CAN-2409, is an off-the-shelf adenovirus product candidate which is combined with the prodrug, valacyclovir, that has generated promising clinical activity across a range of solid tumor indications. CAN-2409 is currently being studied in the following ongoing clinical trials:

- *Prostate Cancer*
  - a Phase 3 randomized, triple-blinded and placebo-controlled clinical trial in the United States under a Special Protocol Assessment (SPA), with the U.S. Food and Drug Administration (FDA) evaluating 711 patients with newly diagnosed, localized prostate cancer who have an intermediate or high-risk for progression. We completed enrollment of this trial in September 2021 and we expect to present topline data at the end of 2024.
  - a Phase 2 randomized, double blind, placebo-controlled clinical trial in the United States evaluating 187 patients with low-to-intermediate risk, localized prostate cancer undergoing active surveillance. We completed enrollment of this trial in June 2019 and we expect topline data from this clinical trial to be available in the fourth quarter of 2024.
- *Non-small Cell Lung Cancer (NSCLC)* – an open-label Phase 2 clinical trial in the United States evaluating CAN-2409 plus valacyclovir in combination with continued PD-(L)1 checkpoint inhibitors in 80 patients with stage III/IV NSCLC who have inadequate response to PD-(L)1 checkpoint inhibitors. We reported initial data from this trial at the American Society for Clinical Oncology (ASCO) Annual Meeting in June 2022 and an update during our Research and Development Day in December 2022, demonstrating the following:
  - Evidence of local and systemic anti-tumor activity
  - Disease control rate of 77% (20/26) in patients entering trial with disease progression (cohort 2)
  - Sustained and ongoing clinical responses greater than 1 year
  - Favorable change in trajectory of tumor progression
  - Decreased tumor size of RECIST target lesions in most patients
  - Reduced uninjected tumor size in 14/21 patients (67%)
  - Overall response rate of 13% (4/30) across cohorts 1 and 2
  - Durable disease stabilization translating into encouraging preliminary evidence of progression-free survival
  - Consistent induction of local and systemic cytotoxic T cell response

- Increased infiltration of CD8+ T cells in the tumor microenvironment
- Systemic expansion of effector T cells and increase in soluble granzyme B levels in peripheral blood
- Favorable safety/tolerability data with most treatment-related adverse events being grade 1/2

We anticipate presenting additional updated clinical data from this ongoing clinical trial in the third quarter of 2023.

- *Pancreatic Cancer* – we have initiated a randomized Phase 2 clinical trial in the United States evaluating CAN-2409 in borderline resectable pancreatic adenocarcinoma. In March 2023, in connection with our cost management and dynamic portfolio management initiatives, we elected to pause new enrollment in this randomized Phase 2 clinical trial, subject to additional funding. Despite the pause in patient enrollment, we continue to expect to present initial clinical data in the fourth quarter of 2023. In a previous Phase 1b trial, patients with pancreatic cancer treated with CAN-2409 in addition to standard of care demonstrated a greater survival duration over the expected survival of the patients treated with the existing standard of care alone in a comparison to historical trial results. Furthermore, in the group of patients where pre- and post-treatment tumor biopsies were available, a statistically significant increase in the number of CD8+ tumor infiltrating lymphocytes was observed.

Our lead HSV-based product candidate, CAN-3110, is currently in an ongoing investigator-sponsored Phase 1 clinical trial in our initial target indication of recurrent high-grade glioma (HGG). These patients have failed standard of care treatment and have a poor prognosis. Initial clinical data from this trial was presented in an oral presentation at the ASCO Annual Meeting in June 2021, and additional biomarker data was reported in November 2021. During our Research and Development Day in December 2022, we presented updated data demonstrating that the treatment was well tolerated with no observed dose-limiting toxicity; achieved 11.6 months mOS with a single dose; and showed evidence of persistent HSV-1 antigen and HSV-1 replication consistent with mechanism of action as well as robust evidence of immune activation.

We are currently evaluating the effects of multiple doses of CAN-3110 in HGG supported by the Break Through Cancer foundation.

We are also designing other novel viral immunotherapy candidates using our proprietary enLIGHTEN™ Discovery Platform, the first systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics to create new viral immunotherapy candidates for solid tumors. In October 2022, we entered into a collaboration with the University of Pennsylvania (Penn) Center for Cellular Immunotherapies to study the impact of novel viral immunotherapy candidates based on Candel's enLIGHTEN™ Discovery Platform to strengthen the activity of Penn's investigational CAR-T cell therapies in difficult to treat solid tumors.

We currently own development and commercialization rights for our programs in major markets, including the United States, Europe and Asia, allowing us to control development and seek approval in those areas as we prepare our commercialization efforts.

We were incorporated in Delaware in June 2003 as Advantagene, Inc. (Advantagene). In December 2019, Advantagene licensed substantially all the assets of Periphagen, a company focused on engineering HSV as a gene therapy vector, and in September 2020, licensed CAN-3110 from Mass General Brigham (MGB). In December 2020, we formally changed our name from Advantagene to Candel Therapeutics, Inc. We completed our initial public offering (IPO) in July 2021.

As of December 31, 2022, we had cash and cash equivalents of $70.1 million, which we believe will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2024.

**Collaborations**

We are a party to a number of license and collaboration agreements under which we license patents, patent applications and other intellectual property to and from third parties.

***Periphagen.*** On December 9, 2019, we entered into a series of agreements, including an exclusive license agreement, a novation agreement, an equipment purchase agreement and an intellectual property assignment agreement, collectively the Periphagen Agreements, with Periphagen, whereby we acquired certain assets and licensed certain rights (including specified patent rights and know-how, or the Licensed IP Rights) of Periphagen, primarily consisting of exclusive rights to their technology platform and a portfolio of pre-clinical, development stage virus vectors. The primary classes of assets are HSV-derived assets expressing neurotrophin-3 (or NT-3 Assets) and other HSV-derived assets (Gene Transfer Neuro-Assets). Under the license agreement, Periphagen granted us a worldwide exclusive license with the right to grant sublicenses through multiple tiers under the Licensed IP Rights to conduct research and to develop, make, have made, use, have used, offer for sale, have sold, export and import products incorporating the Licensed IP Rights in all fields of use except the treatment, diagnosis, and prevention of nononcologic skin diseases and conditions

(including use as an aesthetic). We are currently engaged with Periphagen under a dispute and escalation provision in our exclusive license agreement with Periphagen concerning whether we have used commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset. See Part I, Item 3 “Legal Proceedings”.

***Mass General Brigham (MGB).*** On January 20, 2018, we entered into an exclusive option agreement (the Option Agreement) with MGB. Pursuant to the Option Agreement, we obtained the exclusive right from MGB to negotiate a world-wide, royalty-bearing license to develop and commercialize products covered by certain MGB patents, including those patents covering CAN-3110, in the field of gene therapy and oncolytic vector therapy for the treatment or prevention of cancerous tumors in humans or animals, as such field is further detailed in the Option Agreement (the Licensed Field). In consideration for MGB’s granting of the exclusive option, we paid MGB a non-refundable fee of $40,000.

Under the Option Agreement, we were required to use reasonable efforts to enter into a clinical trial agreement with MGB. We entered into such clinical trial agreement with MGB (MGB Clinical Trial Agreement) on June 19, 2018. Under the MGB Clinical Trial Agreement, we have committed to remitting financial support for the performance of a specified Phase 1 clinical trial by MGB pursuant to a protocol summary contained in the Option Agreement.

On September 15, 2020, we exercised our option and entered into an exclusive patent license agreement with MGB (the MGB License Agreement). Under the MGB License Agreement, MGB granted to us (a) an exclusive, royalty-bearing license under certain of MGB’s patents to make, have made, use, have used, sell and have sold certain products covered by such licensed patents (Licensed Products) and otherwise practice processes covered by such licensed patents (Licensed Processes); and (b) a non-exclusive, royalty-bearing license under certain other of MGB’s patents to make, have made, use, have used, sell and have sold Licensed Products, but not to sell or have sold Licensed Processes. The foregoing rights are sublicensable, subject to sublicensing terms set forth in the MGB License Agreement. In connection with executing the MGB License Agreement, we paid a license issue fee and also agreed to reimburse MGB for all reasonable fees and expenses MGB had incurred and will incur for the preparation, filing, prosecution and maintenance of the licensed patent rights.

***Ventagen.*** On March 1, 2014, we entered into an exclusive license agreement ( the Ventagen Agreement) with Ventagen, a related party. The Ventagen Agreement provides Ventagen an exclusive license, with rights to grant sublicense (subject to certain terms and conditions) under any worldwide patent rights and know-how owned or controlled by us during the term of the Ventagen Agreement which cover applicable technology utilizing the delivery method of the herpes derived TK protein to tumors or other tissues via a viral vector (as further specified therein), to research, use, have used, import, have imported, export, have exported, offer for sale, have sold, sell, distribute and market certain products for the prevention or treatment of cancer in humans and any use in animals (or the Field of Use), or the Licensed Products, for commercial sale and distribution within Mexico, Belize, Guatemala, Honduras, El Salvador, Costa Rica, Nicaragua, Panama, Colombia and Bolivia. Ventagen is 49.5% owned by certain of our stockholders.

**Components of our Results of Operations**

***Revenue***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from sales of products in the foreseeable future. We are recognizing as research and development service revenue $1.0 million that we received in 2014 and 2015 from Ventagen for an exclusive license to develop products for commercial sale and development within certain countries. The $1.0 million is being recognized as revenue over the period during which we provide services under the license agreement.

***Operating Expenses***

Our operating expenses since inception have consisted solely of research and development costs and general and administrative costs.

***Research and Development Expenses***

Research and development expenses consist primarily of costs incurred for our product development activities for our two primary drug candidates, CAN-2409 and CAN-3110. We expense research and development costs as incurred. These include the following:

- employee-related costs, including salaries, benefits and stock-based compensation expense, for personnel engaged in research, development and clinical management functions;
- expenses incurred under agreements with third party clinical sites for the treatment and follow-up for patients enrolled in our clinical trials;

- the cost of acquiring and manufacturing preclinical study materials, including manufacturing registration and validation batches;
- payments made under third-party licensing agreements;
- costs incurred to develop the manufacturing process and capabilities for future clinical trials and commercialization. Our clinical trial material for use in our existing clinical trials was manufactured in prior years;
- costs related to compliance with quality and regulatory requirements;
- costs of outside consultants, primarily related to regulatory; and
- facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and insurance, and other operating costs if specifically identifiable to research and development activities.

We expect that our research and development expenses will continue to increase substantially for the foreseeable future and will comprise a larger percentage of our total expenses as we complete our clinical trials and commence additional clinical trials, continue to discover and develop additional product candidates and develop and scale our manufacturing capabilities. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to increased scale and duration of later stage clinical trials.

We cannot determine with certainty the duration and costs of future clinical trials of CAN-2409 and CAN-3110 or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of, or obtain regulatory approval for, any of our current or future product candidates. The duration, costs, and timing of clinical trials and development of CAN-2409 and CAN-3110 and any other product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials;
- our successful enrollment in and completion of clinical trials, including our ability to generate positive data from any such trials;
- our ability to add and retain key research and development personnel;
- the actual probability of success for our product candidates, including their safety and efficacy, early clinical data, competition, manufacturing capability, and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals;
- the progress of the development efforts of parties with whom we may enter into collaboration agreements, and the terms and timing of any additional collaboration agreements, license or other arrangement, including the timing of any payments thereunder;
- our ability to enter into agreements with CMOs for the commercial manufacture of our product candidate CAN-2409 and the clinical-scale manufacture of our product candidate CAN-3110 as well as complete the qualification of our clinical manufacturing capabilities, internally or through CMOs;
- costs related to manufacturing of our product candidates or to account for any future changes in our manufacturing plans;
- our ability to successfully commercialize our product candidates, if and when approved;
- raising additional funds necessary to complete clinical development of our product candidates;
- our ability to obtain and maintain third-party insurance coverage and adequate reimbursement for our product candidates, if and when approved;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;

- effectively competing with other products if our product candidates are approved;
- the impact of any business interruptions to our operations, including the timing and enrollment of patients in our planned clinical trials, or to those of our manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis;
- our ability to maintain a continued acceptable safety profile for our therapies following approval;
- our ability to obtain and maintain patents, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates, both in the United States and internationally; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates.

***General and Administrative Expenses***

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, business development, and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs including directors and officers insurance; travel expenses; and facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities, and other operating costs that are not specifically attributable to research and development activities.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support our continued clinical development and manufacturing activities and to meet the requirements of a public company. We expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission (SEC) requirements; director and officer insurance costs; and investor and public relations costs.

***Grant Income***

Grant income consists of amounts received under a grant from the National Institute of Health for development of CAN-2409 for use as a therapy for pancreatic cancer.

***Interest, Dividend, and Investment Income***

Interest, dividend and investment income consists of amounts earned on investment of cash equivalents.

***Change in Fair Value of Warrant Liability***

In connection with the November 13, 2018 issuance of Series B preferred stock we issued warrants to the purchasers of the Series B preferred stock, to purchase up to 7,344,968 shares of our common stock with an exercise price of $6.81 per share. We also issued a warrant to the NC Incorporated Ohio Trust, an irrevocable trust funded by us, to purchase 162,740 shares of our common stock, $0.01 par value, at an exercise price of $1.46 per share, subject to adjustments as specified in the warrant agreement (the NC Ohio Warrants). Certain of those warrants are recorded as a liability on our balance sheet. The warrants recorded as a liability are remeasured to their fair value at each reporting date with changes in the fair value recognized as a component of other income (expense), net in the consolidated statements of operations. We will continue to recognize changes in the fair value of the warrants until they are exercised, expire or qualify for equity classification. The fair value of the warrants is determined based on significant inputs not observable in the market. The fair value of the warrants uses various valuation methods, including the Monte Carlo method, the option-pricing method, probability-weighted expected return and the hybrid method, all of which incorporate assumptions and estimates, to value the common stock warrants. The hybrid method is often used when a company is expecting a liquidity event in the near future and is a combination of the option-pricing and probability-weighted expected return methods. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying shares of common stock, risk-free interest rate, expected dividend yield, and the remaining contractual term of the warrants. Therefore, the fair value may not be appropriately captured by simple models.

***Income Taxes***

Since our inception, we have generated cumulative federal and state net operating loss and research and development credit carryforwards for which we have not recorded any net tax benefit due to uncertainty around utilizing these tax attributes within their respective carryforward periods.

As of December 31, 2022, we had gross federal net operating loss carryforwards (NOLs) of approximately $65.9 million and state NOLs of approximately $61.9 million which may be available to offset future taxable income. Our federal NOLs include $8.8 million available to reduce future taxable income through 2028 and approximately $57.1 million of NOLs that do not expire and are available to reduce future taxable income indefinitely. The state NOLs are available to offset future taxable income through 2032. As of December 31, 2022, we also had federal and state research and development tax credit carryforwards of $3.4 million and $1.8 million, respectively, which are available to offset federal and state tax liabilities through 2036 and 2028, respectively.

Realization of future tax benefits is dependent on many factors, including our ability to generate taxable income within the NOL period. Our management has evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets, which are comprised principally of net operating loss carryforwards and certain tax credits. Management has considered our history of cumulative net losses incurred since inception, as well as our lack of product revenue since inception, and has determined that it is more likely than not that we will not realize the benefits of its deferred tax assets. As a result, a full valuation allowance has been established at December 31, 2022.

NOL 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%, as provided under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), as well as under similar state provisions. These ownership changes may limit the amount of NOLs that can be utilized annually to offset future taxable income. In general, an ownership change, as defined under Section 382 of the Code (Section 382), results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. We have completed several financings and not yet determined if such a limitation would be placed against our NOL. We will make such a determination prior to the utilization of any NOL.

**Results of Operations**

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021 (in thousands):

| | YEAR ENDED DECEMBER 31, | | INCREASE/ (DECREASE) |
|---|---|---|---|
| | 2022 | 2021 | |
| Research and development service revenue | $ 125 | $ 125 | $ - |
| Operating expenses: | | | |
| Research and development | 20,787 | 15,178 | 5,609 |
| General and administrative | 14,060 | 10,673 | 3,387 |
| Total operating expenses | 34,847 | 25,851 | 8,996 |
| Loss from operations | (34,722) | (25,726) | 8,996 |
| Grant income | 48 | 1,076 | (1,028) |
| Interest and dividend income (expense), net | (490) | (53) | 437 |
| Change in fair value of warrant liability | 16,370 | (11,421) | 27,791 |
| Net loss | $ (18,794) | $ (36,124) | $ (17,330) |

**Comparison of the Years Ended December 31, 2022 and 2021**

***Revenue***

We had research and development service revenue of $0.1 million for each of the years ended December 31, 2022 and 2021. This represents the recognition as research and development service revenue of a portion of the $1.0 million that we received in 2014 and 2015 from Ventagen, a related party, which is being recognized over the period during which we provide the services.

***Research and Development Expenses***

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

| | YEAR ENDED DECEMBER 31, | | INCREASE |
|---|---|---|---|
| | 2022 | 2021 | (DECREASE) |
| Employee - related | $ 12,688 | $ 8,941 | $ 3,747 |
| Clinical development | 5,608 | 3,828 | 1,780 |
| Depreciation and impairment of fixed assets | 777 | 717 | 60 |
| Pre-clinical research | 629 | 190 | 439 |
| Occupancy | 442 | 584 | (142) |
| Recruiting | 371 | 746 | (375) |
| Other | 272 | 172 | 100 |
| | $ 20,787 | $ 15,178 | $ 5,609 |

Research and development expenses increased $5.6 million from $15.2 million for the year ended December 31, 2021 to $20.8 million for the year ended December 31, 2022. The increase was primarily attributable to a $3.7 million increase in employee compensation costs due to increased research and development headcount, $1.0 million of severance costs, a $1.8 million increase in clinical development costs which was primarily driven by increased manufacturing, clinical, and regulatory costs in support of CAN-2409 programs, and a $0.4 million increase in preclinical costs. These increases were partially offset by a $0.4 million decrease in recruiting expense.

***General and Administrative Expenses***

The following table summarizes our general and administrative expenses for the years ended December 31, 2022 and 2021 (in thousands):

| | YEAR ENDED DECEMBER 31, | | INCREASE |
|---|---|---|---|
| | 2022 | 2021 | (DECREASE) |
| Employee-related | $ 6,455 | $ 5,555 | $ 900 |
| Professional and consulting fees | 3,629 | 2,972 | 657 |
| Insurance | 2,384 | 1,184 | 1,200 |
| Recruiting | 775 | 132 | 643 |
| Occupancy | 184 | 250 | (66) |
| Other | 633 | 580 | 53 |
| | $ 14,060 | $ 10,673 | $ 3,387 |

General and administrative expenses increased $3.4 million from $10.7 million for the year ended December 31, 2021 to $14.1 million for the year ended December 31, 2022. The increase was primarily attributable to a $1.2 million increase in insurance expense due to the cost of director and officers insurance that has been in place since completion of the IPO in 2021, a $0.9 million increase in employee compensation due to increased headcount to manage growth and operate as a public company, $0.7 million increase in professional and consulting fees due to increased legal, accounting, and investor and public relations, and a $0.6 million increase in recruiting expense as a result of bringing on three new members to our board of directors and hiring of a new Chief Financial Officer.

***Grant Income***

Grant income was $48,000 for the year ended December 31, 2022, compared to $1.1 million for the year ended December 31, 2021. Grant income in 2021 represents amounts received under a grant from the National Institutes of Health for development of CAN-2409 for use as a therapy for pancreatic cancer and includes $464,000 for the forgiveness of a Paycheck Protection Plan loan in April 2021. The National Institutes of Health grant for development of CAN-2409 for use as a therapy for pancreatic cancer has expired at the end of 2021. Grant income in 2022 relates to the recognition of income from a grant from the Massachusetts Life Sciences Center.

***Interest, Dividend Expense, Net***

Interest, dividend and expense was $0.5 million for the year ended December 31, 2022 compared to $53,000 for the year ended December 31, 2021, and represents the earnings on our cash equivalents net of interest expense on outstanding debt obligations. The increase is primarily due to increased interest expense incurred as a result of increased borrowing in the first quarter of 2022.

***Change in Fair Value of Warrant Liability***

The change in fair value of our warrant liability was a decrease in the fair value of $16.4 million for the year ended December 31, 2022, compared to an increase in the fair value of $11.4 million for the year ended December 31, 2021. The change in the fair value of the warrant liability is primarily driven by changes in the underlying value of our stock price.

***Liquidity and Capital Resources***

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates. We expect that our research and development and general and administrative costs will continue to increase significantly, including in connection with conducting clinical trials for our product candidates, developing our manufacturing capabilities which may include the cost of establishing a relationship with contract manufacturers to support commercial launch of our product candidate CAN-2409 and costs associated with equipping our laboratory and manufacturing facility to support clinical trials and commercialization and providing general and administrative support for our operations, including the cost associated with operating as a public company. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

We do not currently have any approved products and have never generated any revenue from product sales. We have financed our operations primarily through proceeds from government grants and proceeds from the sale of convertible notes, common stock, and our convertible preferred stock. As of December 31, 2022, we have raised approximately $160.8 million, including $15.6 million of government grants, $66.1 million from the sale of convertible preferred stock, and $79.1 million from the sale of our common stock in our IPO. Our cash and cash equivalents totaled $70.1 million as of December 31, 2022. We had $20.9 million of long-term debt as of December 31, 2022.

On February 24, 2022, the Company entered into a loan and security agreement Loan Agreement with SVB pursuant to which SVB agreed to provide term loans to the Company in an aggregate principal amount of $20.0 million. The Company borrowed $20.0 million upon entering into the Loan Agreement. The Company could have borrowed up to an additional aggregate principal amount not to exceed $5.0 million, at any time on or prior to December 31, 2022, upon the achievement of all of the following milestones, inclusively: (a) positive Phase 2 clinical activity data from the Company's CAN-2409 NSCLC clinical trial, (b) dosing of its first patient in its Phase 3 CAN-2409 high-grade glioma clinical trial; and (c) receipt on or prior to December 31, 2022, of net cash proceeds in an amount equal to at least $75.0 million from the issuance and sale of equity securities to investors acceptable to SVB. The Company did not borrow any of the additional aggregate principal amount on or prior to December 31, 2022. The term loans are secured by substantially all of the Company's properties, rights and assets, except for its intellectual property, which is subject to a negative pledge under the Loan Agreement.

The term loans bear interest at a floating rate per annum equal to the greater of (A) 5.75% and (B) the prime rate (as published in the money rates section of The Wall Street Journal) plus 2.50%. The Company is required to make monthly interest payments, and commencing on February 1, 2024, 24 consecutive installments of principal plus monthly payments of accrued interest. The term loans mature on January 1, 2026. Upon repayment in full of the term loans, the Company will be required to pay a final payment fee equal to 4.50% of the original principal amount of any funded term loan being repaid. The Loan Agreement permits voluntary prepayment of all, but not less than all, of the SVB term loans, subject to a prepayment premium of 1% to 3% based upon the timing of the prepayment.

On August 5, 2022, we filed a shelf registration statement on Form S-3 (the Shelf) with the SEC, which covers the offering, issuance and sale by us of up to an aggregate of $200.0 million of our common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. We simultaneously entered into a sales agreement with Jefferies LLC, as sales agent, to provide for the issuance and sale by us of up to $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf (the ATM Program). The Shelf was declared effective by the SEC on August 12, 2022. As of the date hereof, no sales have been made pursuant to the ATM Program.

As of December 31, 2022, we had cash and cash equivalents of $70.1 million. As a result of prudent cost management and the management of our clinical program portfolio, we believe our cash resources will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2024, compared to our previous expectation of the first quarter of 2024.

**Cash Flows**

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

| | YEARS ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Net cash used in operating activities | $ (31,419) | $ (22,218) |
| Net cash used in investing activities | (1,297) | (1,835) |
| Net cash provided by financing activities | 19,974 | 71,800 |
| Net increase (decrease) in cash and cash equivalents | $ (12,742) | $ 47,747 |

**Cash Flows for the Years Ended December 31, 2022 and 2021**

***Operating Activities***

Net cash used in operating activities for the year ended December 31, 2022 was $31.4 million, primarily consisting of a net loss of $18.8 million as we incurred expenses associated with our clinical programs, we increased our headcount and had costs associated with being a public company in the second half of the year. In addition, we had non-cash income of $16.4 million as a result of the change in the fair value of our warrant liability, which was partially offset by $3.1 million of non-cash stock-based compensation and depreciation expense. Net cash used in operating activities was also impacted by $0.1 million in changes in operating assets and liabilities, primarily driven by an increase of $1.3 million in accrued expenses and a decrease in prepaid expenses and other current assets of $0.4 million. These changes were partially offset by a decrease of $1.2 million in accounts payable and a decrease of $0.5 million in lease-related liabilities.

Net cash used in operating activities for the year ended December 31, 2021 was $22.2 million, primarily consisting of a net loss of $36.1 million as we incurred expenses associated with our clinical programs, increased our headcount and had costs associated with being a public company in the second half of the year. In addition, we had non-cash charges of $14.8 million for the change in the fair value of the warrant liability, stock-based compensation expense, and impairment and depreciation of fixed assets. Net cash used in operating activities was also impacted by $0.9 million in changes in operating assets and liabilities, primarily driven by an increase of $0.7 million in accounts payable, $0.4 million in deferred rent, $0.3 million in accrued expenses, which were offset by an increase of $2.2 million in prepaids and other long term assets.

***Investing Activities***

Net cash used in investing activities for the year ended December 31, 2022 was $1.3 million, which was attributable to the use of $1.3 million for purchases of fixed assets.

Net cash used in investing activities for the year ended December 31, 2021 was $1.8 million, which was attributable to the use of $1.8 million for purchases of fixed assets.

***Financing Activities***

Net cash provided by financing activities for the year ended December 31, 2022 was $20.0 million, primarily consisting of $19.9 million of net proceeds from a term loan with SVB.

Net cash provided by financing activities for the year ended December 31, 2021 was $71.8 million, consisting of $71.3 million in net proceeds from our IPO and $465,000 in proceeds received from warrant and option exercises.

**Funding Requirements**

We expect our operating expenses to increase substantially in the future in connection with our ongoing activities, particularly as we advance CAN-2409 and CAN-3110 through research and development, clinical trials, develop our manufacturing capabilities and build our laboratory and clinical manufacturing facility, as we research and develop additional product candidates including preclinical activities and as we prepare for marketing approval and commercialization. We also expect to incur additional costs associated with operating as a public company.

Specifically, our costs and expenses will increase as we:

- advance the clinical development of CAN-2409 and CAN-3110;
- pursue the preclinical and clinical development of other product candidates using our HSV-based platform;
- develop our manufacturing capabilities, including establishing a relationship with a contract manufacturer for commercial manufacturing of our product candidate CAN-2409 and the construction of our laboratory and clinical manufacturing facility for our product candidate CAN-3110; and

- expand our operational, financial, and management systems and increase personnel, including personnel to support our operations as a public company.
- We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2024. We have based this estimate on assumptions that may prove to be incorrect, and we could utilize our available capital resources sooner than we currently expect.
- Because of the numerous risks and uncertainties associated with the research, development, and commercialization of therapeutics, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:
- the progress, costs, and results of our clinical development and clinical trials for CAN-2409 and CAN-3110;
- the progress, costs, and results of our additional research and preclinical development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and comparable foreign regulatory authorities, if applicable, for our product candidates;
- the costs and timing of internal process development for our manufacturing capabilities;
- the scope, progress, results, and costs of any product candidates that we may derive from our HSV-based platform or with collaborators;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; hire additional personnel in research, manufacturing, and regulatory and clinical development, as well as management personnel;
- the extent to which we in-license or acquire rights to other products, product candidates, or technologies;
- additions or departures of key scientific or management personnel;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution for any of our product candidates for which we obtain marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of operating as a public company.

Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our cash needs through a combination of public or private equity or debt financings and other sources, which may include collaborations strategic alliances and licensing arrangements with third parties. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Debt financing and equity financing, if available, may involve agreements that include restrictive covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business, in addition to those restrictive covenants contained in the Loan Agreement. If we raise additional funds through other sources, such as collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, product development, and research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

**Contractual Obligations and Commitments**

Our primary contractual obligations are our facility lease, the Loan Agreement with SVB, and the Periphagen Note. The table below summarizes the contractual obligations that will become due as of December 31, 2022:

| | PAYMENTS DUE BY PERIOD (in thousands) | | | |
|---|---|---|---|---|
| | TOTAL | LESS THAN 1 YEAR | 1 TO 3 YEARS | 3 TO 5 YEARS |
| Operating lease obligation (1) | $ 2,209 | $ 583 | $ 1,211 | $ 415 |
| Loan Agreement with SVB (2) | 24,350 | $ 2,024 | $ 22,326 | — |
| Periphagen Note (3) | 1,000 | — | — | 1,000 |
| Total | $ 27,559 | $ 2,607 | $ 23,537 | $ 1,415 |

(1) Represents future minimum lease payments under our operating leases for office and laboratory space at our Needham, Massachusetts facility. Our facility lease extends to August of 2026.

(2) Represents future principal and interest payments on our Loan Agreement with SVB, which matures on January 1, 2026.

(3) Represents a $1.0 million promissory note under the terms of our asset purchase agreements with Periphagen, Inc. The promissory note is due upon maturity in November 2027.

See our financial statements included elsewhere in this Annual Report on Form 10-K for additional information on these agreements.

We also enter into contracts in the normal course of business with hospitals, clinics, universities, and other third parties for clinical trials. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancelation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancelation. These payments are not included in the table above as the amount and timing of such payments are not known.

**Critical Accounting Estimates**

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on 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 materially differ from these estimates under different assumptions or conditions.

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

**Accrued Research and Development Expenses**

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

- clinical trial sites where patients are being treated with our product candidates;
- consultants providing services related to process development, regulatory and other services; and
- CMOs who are manufacturing commercial-scale quantities of our product candidates

Actual services performed may vary from our estimates, resulting in adjustments to research and development costs or inventories in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations.

**Determination of Fair Value of Warrants**

In connection with the Series B convertible preferred stock issuance in November 2018, the Company issued warrants to purchase shares of common stock of which certain warrants are shown as a liability on the balance sheet. The fair value of the warrants was determined based on significant inputs not observable in the market. The fair value of the warrants uses various valuation methods, including the Monte Carlo method, the option-pricing method, probability-weighted expected return and the hybrid method, all of which incorporate assumptions and estimates, to value the common stock warrants. The hybrid method is often used when a company is expecting a liquidity event in the near future and is a combination of the option-pricing and probability-weighted expected return methods. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying shares of common stock prior to the IPO, risk-free interest rate, expected dividend yield, expected volatility of the price of the underlying preferred stock, and the remaining contractual term of the warrants. The most significant assumption in the model impacting the fair value of the common stock warrants is the fair value of the Company's common stock as of each remeasurement date. Prior to the IPO, the Company determined the fair value per share of the underlying common stock by taking into consideration the most recent sales of preferred stock, results obtained from third-party valuations and additional factors that were deemed relevant.

**Stock-Based Compensation**

We measure stock options and other stock-based awards granted to our employees, directors, consultants, advisors based on the fair value on the date of the grant, awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards granted to non-employees, compensation expense is recognized over the vesting period which approximates the period over which services are rendered by such non-employees.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the expected volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options, and our expected dividend yield.

**Determination of Fair Value of Common Stock**

Prior to the IPO in July 2021, there had been no public market for our common stock and as such, the estimated fair value of our common stock had been determined by our board of directors as of the date of each option grant, with input from management, taking into consideration our most recently available third-party valuations of common stock at the time of the grants, as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Third-party valuations, or valuation reports, were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

For the December 1, 2020, January 1, 2021, and June 15, 2021 third-party prepared valuation reports, a probability-weighted expected return method was used to determine the fair value of the common stock. The present value of the common stock under each of these three identified scenarios was weighted based on the probability of each scenario occurring to determine the value of the common stock. These third-party valuations resulted in a valuation of our common stock of $3.96, $4.97 and $6.64 per share as of December 1, 2020, January 1, 2021 and June 15, 2021, respectively.

In addition to considering the results of the valuation reports, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of convertible preferred stock and the superior rights and preferences of the convertible preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biotechnology industry and trends within that industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our convertible preferred stock;

- the likelihood of achieving a liquidity event, such as an initial public offering or sale of our company considering prevailing market conditions; and
- the analysis of initial public offerings and the market performance of similar companies in the biotechnology industry.

The assumptions underlying these valuations were highly complex and subjective and represented management's best estimates, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could be materially different.

Subsequent to the IPO, a public trading market for our common stock has been established and it is no longer necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock is determined based on the quoted market price of our common stock.

**Recent Accounting Pronouncements**

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations, or cash flows is disclosed in Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on form 10-K.

**Emerging Growth Company Status**

In April 2012, the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or an EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended (the Securities Act) for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

## Inflation

Inflation has increased during the periods covered by this Annual Report, and is expected to continue to increase for the near future. Inflationary factors, such as increases in the cost of our product components, interest rates and overhead costs may adversely affect our operating results. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience some effect in the future, especially if inflation rates continue to rise.

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

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, and are not required to provide the information under this item.

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

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear beginning on page F-1 of this Annual Report for the year ended December 31, 2022.

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

None

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

**Limitations on Effectiveness of Controls and Procedures**

Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

**Evaluation of Disclosure Controls and Procedures**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Securities and Exchange Act of 1934, as amended). We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’s rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

**Management's Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over 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, a company’s principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company’s board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of 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 a company’s 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 a company’s receipts and expenditures are being made only in accordance with authorizations of the company’s management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Under the supervision of and with the participation of our principal executive officer and principal financial

officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on internal control over financial reporting due to an exemption established by the JOBS Act for “emerging growth companies.”

**Remediation of Previously Reported Material Weaknesses**

The material weaknesses related to our finance and accounting staff and segregation of duties that were previously reported in Item 9A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and 2020 and are described in "Risk factors" section of the Annual Report on Form 10-K were remediated during our fiscal year ended December 31, 2022, and we determined that we maintained effective internal controls over our financial reporting as of December 31, 2022.

Management took significant steps to remediate the control deficiencies that led to the material weaknesses and has been actively engaged in remediating the previously identified material weaknesses. The following remedial actions have been taken during the year ended December 31, 2022:

1. In September 2022, we hired a new Chief Financial Officer with prior experience serving as a chief financial and accounting officer of several public companies who also served ten years in a major public accounting firm. We hired a Controller in November 2021 with experience working at a public company and as a manager at a major public accounting firm. Each of the above personnel have technical accounting expertise and experience with the internal control, compliance and financial reporting requirements of companies subject to PCAOB standards.
2. We strengthened supervisory reviews by our financial management.
3. We expanded our accounting and finance team to add additional qualified accounting and finance resources, including augmenting our finance team with third-party consultants that possess the required expertise to assist management with their review, as necessary.
4. We implemented Oracle NetSuite as our Enterprise Resource Planning (ERP) solution in the third quarter of 2022, which among other features, has automated segregation of duties functionality relating to the ability to create and post journal entries to our general ledger.
5. We implemented a Software-as-a-Service (SAAS) solution to assist with the review and approval of account reconciliations and other financial close workflows.
6. We enhanced business process narratives and identification of key controls in our SOX framework.
7. We performed internal interim and year-end SOX assessments that did not result in the identification of any material weaknesses related to the design or operating effectiveness of identified key controls.

We believe the above actions were effective and concluded that the material weaknesses described above were remediated as of December 31, 2022.

The process of implementing an effective financial reporting system is a continuous effort that requires us to anticipate and react to changes in our business and the economic and regulatory environments and to expend significant resources to maintain a financial reporting system that is adequate to satisfy our reporting obligations. .

**Changes in Internal Control Over Financial Reporting**

Except for the remedial actions described above, there was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) that occurred during the three months ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting

**Item 9B. Other Information.**

None.

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

Not applicable.

## PART III

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

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 11. Executive Compensation.**

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence.**

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services.**

Our independent public accounting firm is KPMG LLP, Boston, Massachusetts, PCAOB Auditor ID 185

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

## PART IV

**Item 15. Exhibits, Financial Statement Schedules.**

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

**Exhibits:**

| Exhibit Number | Description |
|---|---|
| 3.1 | Amended and Restated Certificate of Incorporation of Candel Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on July 30, 2021) |
| 3.2 | Amended and Restated Bylaws of Candel Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the SEC on July 30, 2021) |
| 4.1 | Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 4.2 | Description of Securities (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K filed with the SEC on March 29, 2022) |
| 4.3 | Investors' Rights Agreement (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on June 25, 2021) |
| 4.4 | Form of November 2018 Unconditional Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 4.5 | Form of November 2018 Conditional Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 4.6 | Form of Warrant to Purchase Series A Convertible Preferred Stock (incorporated by reference to Exhibit 4.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on June 25, 2021) |
| 10.1# | 2015 Stock Plan, as amended, and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.2# | 2021 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.3# | Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.4# | Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.5.1# | Employment Agreement by and between Advantagene, Inc. d/b/a Candel Therapeutics and Paul Peter Tak, M.D., Ph.D. dated September 12, 2020 (incorporated by reference to Exhibit 10.5.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.5.2# | Amended and Restated Employment Agreement by and between Advantagene, Inc. and Estuardo Aguilar-Cordova dated November 13, 2018 (incorporated by reference to Exhibit 10.5.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.5.3# | Amended and Restated Employment Agreement by and between Advantagene, Inc. and Laura Aguilar, M.D., Ph.D. dated November 13, 2018 (incorporated by reference to Exhibit 10.5.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.5.4# | Employment Agreement by and between Advantagene, Inc. d/b/a Candel Therapeutics and John Canepa dated December 1, 2020 (incorporated by reference to Exhibit 10.5.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |

| | |
|---|---|
| 10.5.5# | Employment Agreement by and between Advantagene, Inc. d/b/a Candel Therapeutics and Nathan Caffo dated September 24, 2020 (incorporated by reference to Exhibit 10.5.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333-257444) filed with the SEC on July 16, 2021) |
| 10.6# | Form of Indemnification Agreement (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.7 | Exclusive License Agreement by and between Advantagene, Inc. and Ventagen, LLC dated March 1, 2014 (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.8 | Exclusive License Agreement by and between Advantagene, Inc., d/b/a Candel Therapeutics and Periphagen, Inc. dated December 9, 2019 (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.9 | Exclusive Patent License Agreement by and between Advantagene, Inc. and Mass General Brigham (formerly known as The Brigham and Women's Hospital, Inc.) dated September 15, 2020 (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.10 | Lease of Premises at 117 Kendrick Street, Needham, Massachusetts by and between 117 Kendrick DE, LLC and the Registrant dated as of February 4, 2019 (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333- 257444) filed with the SEC on July 16, 2021) |
| 10.11 | Loan and Security Agreement by and between the Registrant and Silicon Valley Bank, dated February 24, 2022 (incorporated by reference to Exhibit 10.11 to the Registrant's Annual Report on Form 10-K filed with the SEC on March 29, 2022) |
| 10.12# | Employment Agreement by and between Candel Therapeutics and Francesca Barone dated February 3, 2022 (incorporated by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K filed with the SEC on March 29, 2022) |
| 10.13# | Consulting Agreement by and between Candel Therapeutics, Inc. and Susan Stewart dated October 19, 2021 (incorporated by reference to Exhibit 10.13 to the Registrant's Annual Report on Form 10-K filed with the SEC on March 29, 2022) |
| 10.14# | Employment Agreement by and between Candel Therapeutics and Seshu Tyagarajan dated April 14, 2022 (incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q filed with the SEC on May 12, 2022) |
| 10.15# | Employment Agreement by and between Candel Therapeutics and Jason A. Amello dated September 21, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the SEC on November 10, 2022) |
| 10.16* | Master Production Services Agreement by and between Candel Therapeutics and SAFC Carlsbad, Inc., effective November 3, 2022 |
| 21.1 | List of Subsidiary (incorporated by reference to Exhibit 21.1 to the Registrant's Annual Report on Form 10-K filed with the SEC on March 29, 2022) |
| 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*+ | Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 |
| 101.INS | Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document. |
| 101.SCH | Inline XBRL Taxonomy Extension Schema Document |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB | Inline XBRL Taxonomy Extension Label Linkbase Document |
| 101.PRE | Inline XBRL Taxonomy Extension Presentation Linkbase Document |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

* Filed herewith.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report on form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

# Indicates a management contract or any compensatory plan, contract or arrangement

**Item 16. Form 10-K Summary**

None.

## INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

## Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Candel Therapeutics, Inc.:

*Opinion on the Consolidated Financial Statements*

We have audited the accompanying consolidated balance sheets of Candel Therapeutics, Inc. and subsidiary (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

*Change in Accounting Principle*

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2022 due to the adoption of Accounting Standards Update No. 2016-02, *Leases (Topic 842)* and Accounting Standards Update No. 2018-11, *Leases (Topic 842): Targeted Improvements.*

*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.

/s/ KPMG LLP

We have served as the Company's auditor since 2019

Boston, Massachusetts
March 30, 2023

**CANDEL THERAPEUTICS, INC.**

**Consolidated Balance Sheets**
(In thousands, except share and per share amounts)

| | DECEMBER 31, | |
|---|---|---|
| | **2022** | **2021** |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 70,058 | $ 82,642 |
| Prepaid expenses and other current assets | 1,887 | 2,303 |
| **Total current assets** | 71,945 | 84,945 |
| Fixed assets, net | 4,424 | 3,836 |
| Lease right of use assets | 1,056 | — |
| Restricted cash | 266 | 424 |
| **Total assets** | $ 77,691 | $ 89,205 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 380 | $ 1,590 |
| Accrued expenses | 4,723 | 3,438 |
| Current portion of lease liability | 464 | — |
| Other current liabilities | 48 | 334 |
| **Total current liabilities** | 5,615 | 5,362 |
| Deferred revenue | 144 | — |
| Deferred rent | — | 894 |
| Term loan payable to a bank | 20,202 | — |
| Other long-term debt | 648 | 560 |
| Lease liability, net of current portion | 1,486 | — |
| Warrant liability | 1,882 | 18,252 |
| **Total liabilities** | 29,977 | 25,068 |
| Commitments and contingencies (Note 15) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.01 par value; 10,000,000 shares authorized at December 31, 2022 and 2021; no shares issued or outstanding at December 31, 2022 and 2021, respectively. | — | — |
| Common stock, $0.01 par value; 150,000,000 shares authorized at December 31, 2022 and 2021; 29,042,418 and 28,689,842 shares issued at December 31, 2022 and 2021, respectively; and 28,919,810 and 28,689,842 shares outstanding at December 31, 2022 and 2021, respectively. | 290 | 286 |
| Treasury stock (at cost) | (448) | — |
| Additional paid-in capital | 146,961 | 144,146 |
| Accumulated deficit | (99,089) | (80,295) |
| **Total stockholders' equity** | 47,714 | 64,137 |
| **Total liabilities and stockholders' equity** | $ 77,691 | $ 89,205 |

The accompanying notes are an integral part of these consolidated financial statements.

**CANDEL THERAPEUTICS, INC.**

**Consolidated Statements of Operations**
(In thousands, except share and per share amounts)

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | **2022** | **2021** |
| **Research and development service revenue, related party** | $ 125 | $ 125 |
| **Operating expenses:** | | |
| Research and development | 20,787 | 15,178 |
| General and administrative | 14,060 | 10,673 |
| **Total operating expenses** | 34,847 | 25,851 |
| **Loss from operations** | (34,722) | (25,726) |
| **Other income (expense):** | | |
| Grant income | 48 | 1,076 |
| Interest and dividend income (expense), net | (490) | (53) |
| Change in fair value of warrant liability | 16,370 | (11,421) |
| **Total other income (expense), net** | 15,928 | (10,398) |
| **Net loss** | $ (18,794) | $ (36,124) |
| **Net loss per share, basic and diluted** | $ (0.65) | $ (1.91) |
| **Weighted-average common shares outstanding, basic and diluted** | 28,823,480 | 18,873,048 |

The accompanying notes are an integral part of these consolidated financial statements.

| | SERIES B CONVERTIBLE PREFERRED STOCK | | SERIES C CONVERTIBLE PREFERRED STOCK | | COMMON STOCK | | TREASURY STOCK | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | SHARES | AMOUNT | SHARES | AMOUNT | SHARES | AMOUNT | SHARES | AMOUNT | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED DEFICIT | STOCKHOLDERS' EQUITY (DEFICIT) |
| **Balance as of December 31, 2020** | 11,155,506 | $ 26,560 | 6,032,170 | $ 22,500 | 11,635,094 | $ 116 | — | $ — | $ 20,493 | $ (44,171) | $ (23,562) |
| Options exercised | — | — | — | — | 24,410 | — | — | — | 35 | — | 35 |
| Warrants exercised | — | — | — | — | 75,946 | 1 | — | — | 429 | — | 430 |
| Stock-based compensation | — | — | — | — | — | — | — | — | 2,588 | — | 2,588 |
| Change in fair value of NC Ohio Trust Warrants | — | — | — | — | — | — | — | — | 375 | — | 375 |
| Conversion of Series B Preferred Stock to Common Stock | (11,155,506) | (26,560) | — | — | 4,538,578 | 45 | — | — | 26,515 | — | 26,560 |
| Conversion of Series C Preferred Stock to Common Stock | — | — | (6,032,170) | (22,500) | 2,527,820 | 25 | — | — | 22,475 | — | 22,500 |
| Proceeds from IPO, net | — | — | — | — | 9,887,994 | 99 | — | — | 71,236 | — | 71,335 |
| Net loss | — | — | — | — | — | — | — | — | — | (36,124) | (36,124) |
| **Balance as of December 31, 2021** | — | $ — | — | $ — | 28,689,842 | $ 286 | — | $ — | $ 144,146 | $ (80,295) | $ 64,137 |
| Options exercised | — | — | — | — | 352,576 | 4 | — | — | 508 | — | 512 |
| Treasury stock acquired | — | — | — | — | — | — | (122,608) | (448) | — | — | (448) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 3,145 | — | 3,145 |
| Change in fair value of NC Ohio Trust Warrants | — | — | — | — | — | — | — | — | (838) | — | (838) |
| Net loss | — | — | — | — | — | — | — | — | — | (18,794) | (18,794) |
| **Balance as of December 31, 2022** | — | $ — | — | $ — | 29,042,418 | $ 290 | (122,608) | $ (448) | $ 146,961 | $ (99,089) | $ 47,714 |

The accompanying notes are an integral part of these consolidated financial statements.

**CANDEL THERAPEUTICS, INC.**

**Consolidated Statements of Cash Flows**
(In thousands, except share and per share amounts)

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | **2022** | **2021** |
| **Cash Flows from Operating Activities:** | | |
| Net loss | **$ (18,794)** | **$ (36,124)** |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation and amortization | 778 | 232 |
| Impairment on manufacturing equipment | — | 553 |
| Non-cash stock compensation expense | 2,307 | 2,963 |
| Non-cash lease expense | 209 | — |
| Non-cash interest expense | 89 | 76 |
| Change in fair value of warrant liability | (16,370) | 11,421 |
| Accretion of debt discount | 291 | — |
| Paycheck protection program loan forgiveness | — | (463) |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | 416 | (2,210) |
| Other long term assets | — | 83 |
| Accounts payable | (1,213) | 669 |
| Accrued expenses | 1,265 | 297 |
| Deferred revenue | 67 | (125) |
| Deferred rent | — | 410 |
| Lease liability | (464) | — |
| Net cash used in operating activities | **(31,419)** | **(22,218)** |
| **Cash Flows from Investing Activities:** | | |
| Purchase of fixed assets | (1,297) | (1,835) |
| Net cash used in investing activities | **(1,297)** | **(1,835)** |
| **Cash Flows from Financing Activities:** | | |
| Net proceeds from initial public offering | — | 71,335 |
| Net proceeds from bank term loan | 19,910 | — |
| Proceeds from option exercises | 64 | 35 |
| Proceeds from warrant exercises | — | 430 |
| Net cash provided by financing activities | **19,974** | **71,800** |
| Net increase (decrease) in cash | **(12,742)** | **47,747** |
| Cash, cash equivalents and restricted cash at beginning of period | **83,066** | **35,319** |
| Cash, cash equivalents and restricted cash at end of period | **$ 70,324** | **$ 83,066** |
| **Supplemental cash flow information:** | | |
| Cash paid for taxes | $ 183 | $ 29 |
| Cash paid for interest | $ 1,152 | $ — |
| **Supplemental disclosures of non-cash information:** | | |
| Lease liability arising from obtaining right-of-use assets | $ 2,368 | $ — |
| Capital expenditures in accounts payable and accrued expenses | $ 69 | $ — |
| Common stock exchange for option exercise | $ 448 | $ — |

The accompanying notes are an integral part of these consolidated financial statements.

## 1. Organization and Basis of Presentation

Candel Therapeutics, Inc., formerly known as Advantagene, Inc. (the Company) is a late clinical stage biotechnology company that was incorporated in Delaware in June 2003. On November 30, 2020, the Company changed its name to Candel Therapeutics, Inc. The Company is focused on developing and commercializing viral immunotherapies to help patients fight cancer. The Company's engineered viruses are designed to induce immunogenic cell death through direct viral – mediated cytotoxicity in cancer cells, thus releasing tumor neo-antigens and creating a pro-inflammatory microenvironment at the site of injection. The Company has established two clinical stage viral immunotherapy platforms and its two product candidates, CAN-2409 and CAN-3110, are in clinical trials for a number of tumor types. In addition, the Company recently announced a collaboration with the University of Pennsylvania (Penn) to study the impact of novel viral immunotherapies based on Candel's propriety enLIGHTEN™ Discovery Platform to strengthen the effects of Penn's investigational CAR-T cell therapies in solid tumor models.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

The Company has funded its operations primarily with proceeds from the sale of its convertible notes and capital stock and from debt borrowings. The Company has incurred recurring losses since its inception, including a net loss of $18.8 million and $36.1 million for the years ended December 31, 2022, and 2021, respectively. In addition, as of December 31, 2022, the Company had an accumulated deficit of $99.1 million. The Company expects to continue to generate operating losses for the foreseeable future.

On July 29, 2021, the Company completed its initial public offering of common stock (the IPO) at which time the Company issued 9,000,000 shares of its common stock at a price to the public of $8.00 per share, and on August 13, 2021, the Company issued an additional 887,994 shares of common stock at $8.00 per share as a partial exercise of the underwriters' option to purchase additional shares, resulting in net proceeds to the Company of $71.3 million, after deducting underwriting discounts and commissions and offering expenses. Upon closing of the IPO, all outstanding shares of the Company's convertible preferred stock automatically converted into 7,066,398 shares of common stock.

On August 5, 2022, the Company filed a shelf registration statement on Form S-3 (the Shelf) with the SEC, which covers the offering, issuance, and sale by us of up to an aggregate of $200.0 million of our common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. We simultaneously entered into a sales agreement with Jefferies LLC, as sales agent, to provide for the issuance and sale by us of up to $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf (the ATM Program). The Shelf was declared effective by the SEC on August 12, 2022. As of the date hereof, no sales have been made pursuant to the ATM Program.

The future viability of the Company is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurances that additional funding will be available on terms acceptable to the Company, or at all. The Company believes that existing resources will fund planned operations for at least 12 months from the date that these consolidated financial statements were available to be issued.

Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company continues as a going concern and contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

## 2. Summary of Significant Accounting Policies

### *Basis of Presentation*

The accompanying consolidated financial statements have been prepared in accordance with accounting standards set by the Financial Accounting Standards Board (FASB). The FASB sets generally accepted accounting principles (GAAP) that the Company follows to ensure its financial condition, results of operations, and cash flows are consistently

reported. References to GAAP issued by the FASB in these notes to the financial statements are to the FASB Accounting Standards Codification (ASC).

***Principles of Consolidation***

The consolidated financial statements include the accounts of Candel Therapeutics, Inc. and its wholly owned subsidiary Candel Therapeutics Securities Corporation. All intercompany transactions and balances have been eliminated.

***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 in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision maker, the Company's chief executive officer, views the Company's operations and manages its business as a single operating segment. The Company only operates in the United States.

***Emerging Growth Company***

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the Jobs Act). Under the Jobs Act emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the Jobs Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that is (i) no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the Jobs Act. As a result, these consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

***Use of Estimates***

The preparation of the Company’s consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and related disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of revenue and expenses during the reporting period. On an ongoing basis, the Company’s management evaluates its estimates, which include but are not limited to management’s judgments of accrued expenses, valuation of stock-based option awards, valuations of warrants, and income taxes. Actual results could differ from those estimates.

Prior to the IPO, the Company utilized significant estimates and assumptions in determining the fair value of its common stock. The Company has utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation (the Practice Aid), to estimate the fair value of its common stock and warrants. Each valuation methodology includes estimates and assumptions that require the Company’s judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company’s common stock at the time of, and the likelihood of, achieving a liquidity event, such as an initial public offering or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

***Cash and Cash Equivalents***

The Company considers all highly liquid investments purchased with original final maturities of 90 days or less from the date of purchase to be cash equivalents. Cash and cash equivalents comprise marketable securities with maturities of less than 90 days when purchased. Cash equivalents are reported at fair value.

***Restricted Cash***

The Company has $0.3 million and $0.4 million of restricted cash as of December 31, 2022 and 2021, respectively, which represents cash held as a security deposit under the terms of the Company’s Needham, Massachusetts facility lease and at December 31, 2021, as security for the Company credit card.

***Fair Value Measurements***

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the

use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The carrying values of cash and cash equivalents (considered as Level 1 measurement), accounts payable, and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities. The Company's warrant liability is carried at fair value and is classified as Level 3 measurement.

***Property and Equipment***

Property and equipment consist of laboratory and manufacturing equipment, networking and computer equipment, furniture and fixtures and leasehold improvements. Property and equipment are recorded at cost, and depreciated using the straight-line method over the estimated useful lives of the respective assets:

| ASSET | ESTIMATED USEFUL LIFE |
|---|---|
| Networking and computer equipment | 5 years |
| Laboratory equipment | 5 years |
| Manufacturing equipment | 5 years |
| Furniture and fixtures | 5 years |
| Leasehold improvements | Shorter of the useful life or remaining lease term |

***Leases***

The Company adopted ASC 842 as of January 1, 2022 and elected the transition method under ASU 2016-02 whereby the Company records a right-of-use asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. The Company also elected to apply the practical expedients intended to ease transition. Accordingly, the Company has only applied ASC 842 to leases existing as of January 1, 2022. The Company determines if an arrangement is, or contains, a lease at inception.

Lease right of use assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Lease right of use assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments to be made over the lease term. The lease right of use asset is equal to the lease liability and adjusted for prepaid rent, initial direct costs, and incentives. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term. The Company has elected to not apply the recognition requirements of ASC 842 for short-term leases, which is defined as a lease that, at the lease commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the Company is reasonably certain to exercise.

For real estate lease agreements entered into or modified after the adoption of ASC 842 that include lease and non-lease components, the Company has elected to account for the lease and non-lease components, such as common area maintenance charges, as a single lease component term.

***Concentrations of Credit Risk***

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and marketable securities. Periodically, the Company maintains deposits and investments in accredited financial institutions in-excess of the federally insured limits. The Company deposits its cash in financial institutions with a high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal risk associated with commercial banking relationships.

***Impairment of Long-lived Assets***

Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. Long-lived assets consist of fixed assets and operating lease assets.

In the fourth quarter of 2021, the Company recorded an impairment charge of approximately $0.6 million related to manufacturing equipment that the Company does not plan to use for its intended use and recorded a reserve to reduce the carrying value to its estimated realizable value. The Company has not recorded any additional impairment losses on such long-lived assets.

***Revenue Recognition***

The Company applies Accounting Standards Codification (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, such as leases, insurance, collaboration arrangements and financial instruments. 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. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and then assesses whether or not each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

***Research and Development Costs and Accruals***

Research and development expenses include salaries and benefits, materials and supplies, preclinical and clinical trial expenses, stock-based compensation expense, depreciation of equipment, contract services and other outside expenses. The Company has entered into various research and development-related contracts with clinical and research institutions, contract research organizations, and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. Costs of certain development activities, such as manufacturing, pre-clinical and clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs incurred in obtaining technology licenses and intellectual property are charged to research and development expenses as acquired in-process research and development if the technology licensed or intellectual property acquired has not reached technological feasibility and has no alternative future use.

***Patent Costs***

All patent-related costs incurred in connection with preparing, filing, maintaining and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified in general and administrative expenses.

***Stock-Based Compensation***

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, Compensation—Stock Compensation (ASC 718). ASC 718 requires all share-based payments to employees and directors to be recognized as expense in the consolidated statements of operations based on their grant date fair values. In addition, in accordance with FASB Accounting Standards Update (ASU) 2016-09 which identifies areas for simplification of several areas of share-based payment transactions, the Company treats non-employee grants the same as employee grants. The

Company estimates the fair value of options granted using the Black-Scholes option pricing model for stock option grants to both employees and non-employees. The Company believes the fair value of the stock options granted to non-employees is more reliably determinable than the fair value of the services provided.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to a lack of company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the share-based payment as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

Prior to the IPO, there were significant judgments and estimates inherent in the determination of the fair value of the Company's common stock. These estimates and assumptions included a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to its common stock at the time of, and the likelihood of, achieving a liquidity event, such as an initial public offering or sale.

The Company generally expenses the fair value of its share-based compensation awards to employees and non-employees on a straight-line basis over the requisite service period, which is generally the vesting period.

***Government Grants***

The Company has applied for grants for the reimbursement of expenditures with the National Institutes of Health (NIH) and the Massachusetts Life Sciences Center for certain qualified operating expenditures, including employee-related costs. The Company recognizes government grants when there is reasonable assurance that the Company will comply with the conditions attached to the grant arrangement and the grant will be received.

Government grants for research and development efforts are recorded as grant income and classified in other income in the consolidated statements of operations. The Company recognized government grants of $48,000 and $1.1 million for the years ended December 31, 2022 and 2021, respectively. Grant income is recognized as a component of other income/(expense), net in the consolidated statements of operations. The Company's grant with the NIH was completed at the end of 2021. The Company's grant with the Massachusetts Life Sciences Center began in 2022.

***Income Taxes***

The Company accounts for income taxes using the asset and liability method in accordance with ASC Topic 740, Income Taxes (ASC 740) which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies. At December 31, 2022 and 2021, the Company has concluded that a full valuation allowance is necessary for its deferred tax assets (see Note 12).

The Company accounts for uncertainty in income taxes, by applying the two-step process to determine the amount of tax benefit to be recognized in the financial statements. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax is then assessed as the amount of benefits to be recognized in the consolidated financial statements. The amount of benefits that may be used are the largest amounts that have a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of

any resulting tax reserves or unrecognized tax benefits that are considered appropriate as well as the related net interest received.

***Net Loss Per Share***

Basic net loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. In periods where the Company reports a net loss attributable to common stockholders, diluted net loss per share is the same as basic net loss per share, since dilutive shares of common stock are not assumed to have been issued if their effect is anti-dilutive. Diluted net loss per share is the same as basic net loss per share for the years ended December 31, 2022 and 2021 since all potential shares of common stock instruments are anti-dilutive as a result of the loss for such periods.

***Recently Adopted Accounting Standards***

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) (ASU 2016-02), as amended by various subsequently issued ASUs. The standard requires lessees to recognize an operating lease with a term greater than one year on their balance sheets as a right-of-use asset and corresponding lease liability, measured at the present value of the lease payments. Lessees are required to classify leases as either finance or operating leases. If the lease is effectively a financed purchase by the lessee, it is classified as a financing lease, otherwise it is classified as an operating lease. This classification will determine the pattern of recognition of lease cost on our consolidated statement of operations over the term of the lease.

In July 2018, the FASB also issued ASU 2018-11, Leases (Topic 842): Targeted Improvements (ASU 2018-11), which permits entities to continue applying legacy guidance in ASC 840, Leases, including its disclosure requirements, in the comparative periods presented in the year that the entity adopts the new leasing standard. The Company elected the package of practical expedients permitted under the transition guidance within the standard. Accordingly, the Company did not reassess the conclusion of whether the existing arrangements contain a lease, lease classification and initial direct costs under ASC 842.

In June 2020, the FASB also issued ASU 2020-05, Revenue from contracts with customers (Topic 606) and Leases (Topic 842): effective dates for certain entities, which deferred the effective date certain entities were required to adopt ASC 842. The update extended the effective date for adoption of ASC 842 until fiscal years beginning after December 15, 2021. As an emerging growth company we were not required to adopt ASC 842 until January 1, 2022. The Company adopted the standard on January 1, 2022 using the effective date method. As such, the consolidated balance sheets and statements of operations for prior periods will not be comparable in the year of adoption of ASC 842.

As a result of the adoption of ASC 842, the Company recorded a lease right of use asset of $1.3 million and a lease liability of $2.4 million on the consolidated balance sheets as of January 1, 2022 related to an operating lease. The Company derecognized deferred rent liabilities, which makes up the difference between the lease right of use asset and lease liability. The adoption of the standard did not have a material impact on the Company’s consolidated statement of operations or consolidated statement of cash flows.

In August 2020, the FASB issued ASU 2020-06, Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging - Contracts in Entity's Own Equity (Subtopic 815-40). The guidance simplifies the complexity associated with applying U.S. GAAP for certain financial instruments with characteristics of liabilities and equity. This ASU (1) simplifies the accounting for convertible debt instruments and convertible preferred stock by removing guidance in ASC 470-20, Debt: Debt with Conversion and Other Options, that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock; (2) revises the scope exception from derivative accounting in ASC 815-40 for freestanding financial instruments and embedded features that are both indexed to the issuers own stock and classified in stockholders' equity, by removing certain criteria required for equity classification; and (3) revises the guidance in ASC 260, Earnings Per Share, to require entities to calculate diluted earnings per share for convertible instruments by using the if-converted method. As an emerging growth company, we are not required to adopt ASU 2020-06 until January 1, 2024, however early adoption is permitted. The Company elected to early adopt the standard on January 1, 2022 and upon adoption, there was no impact to our consolidated statement of operations and cash flows and our basic and diluted net loss per share amounts.

In November 2021, the FASB issued ASU 2021-10, which created Topic 832, Government Assistance, which requires business entities to disclose information about certain government assistance they receive. The ASU requires qualitative and quantitative disclosures around the nature of transactions and related accounting policy used, the line items on the balance sheet and income statement that are affected, and the significant terms and conditions of the transactions. The ASU is effective for fiscal years beginning after December 15, 2021. The Company believes its

historical disclosure already met the requirements of the new standard. As such, no changes or additional disclosure was determined to be necessary.

**3. Fair Value of Financial Assets and Liabilities**

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

| | FAIR VALUE MEASUREMENTS AS OF DECEMBER 31, 2022 USING: | | | |
|---|---|---|---|---|
| | LEVEL 1 | LEVEL 2 | LEVEL 3 | TOTAL |
| **Liabilities:** | | | | |
| Warrant liability | — | — | 1,882 | 1,882 |
| Total | $ — | $ — | $ 1,882 | $ 1,882 |

| | FAIR VALUE MEASUREMENTS AS OF DECEMBER 31, 2021 USING: | | | |
|---|---|---|---|---|
| | LEVEL 1 | LEVEL 2 | LEVEL 3 | TOTAL |
| **Liabilities:** | | | | |
| Warrant liability | — | — | 18,252 | 18,252 |
| Total | $ — | $ — | $ 18,252 | $ 18,252 |

***Valuation of Warrant Liability***

In connection with the November 13, 2018 issuance of Series B convertible preferred stock, the Company issued warrants to purchase shares of common stock of which certain warrants are shown as a liability on the balance sheet, see Note 10. The fair value of the warrant liability was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the warrant liability uses various valuation methods, including the Monte Carlo method, the option-pricing method, probability-weighted expected return and the hybrid method, all of which incorporate assumptions and estimates, to value the common stock warrants. The hybrid method is often used when a company is expecting a liquidity event in the near future and is a combination of the option-pricing and probability-weighted expected return methods. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying shares of common stock, risk-free interest rate, expected dividend yield, expected volatility of the price of the underlying common stock, and the remaining contractual term of the warrants. The most significant assumption in the model impacting the fair value of the common stock warrants is the fair value of the Company's common stock as of each remeasurement date. Prior to the IPO, the Company determined the fair value per share of the underlying common stock by taking into consideration the most recent sales of preferred stock, results obtained from third-party valuations and additional factors that are deemed relevant.

The following table provides a roll forward of the aggregate fair values of the Company's warrant liability, for which fair value is determined by Level 3 inputs (in thousands):

| | SERIES B WARRANT LIABILITY |
|---|---|
| Balance at December 31, 2020 | $ 6,831 |
| Change in fair value | 11,421 |
| Balance at December 31, 2021 | $ 18,252 |
| Change in fair value | (16,370) |
| Balance at December 31, 2022 | $ 1,882 |

**4. Fixed Assets, Net**

Fixed assets, net consisted of the following (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Laboratory equipment | $ 1,055 | $ 77 |
| Manufacturing equipment | 1,201 | 933 |
| Furniture and fixtures | 159 | 112 |
| Networking and computer equipment | 81 | 72 |
| Leasehold improvements | 3,057 | 2,994 |
| Total fixed assets | $ 5,553 | $ 4,188 |
| Less accumulated depreciation | (1,129) | (352) |
| **Fixed assets, net** | $ 4,424 | $ 3,836 |

Depreciation and amortization expense was $0.8 million and $0.2 million for the years ended December 31, 2022 and 2021, respectively.

**5. Accrued Expenses**

Accrued expenses consisted of the following (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Payroll and employee related expenses | $ 2,647 | $ 2,096 |
| Third-party research and development expenses | 1,486 | 632 |
| Professional fees and other | 590 | 710 |
| | $ 4,723 | $ 3,438 |

**6. Term Loan**

On February 24, 2022, the Company entered into a four-year loan and security agreement (the Loan Agreement) with Silicon Valley Bank (SVB) pursuant to which SVB has agreed to provide term loans to the Company in an aggregate principal amount of up to $25.0 million. The Company borrowed $20.0 million upon entering into the Loan Agreement. The Company could have borrowed up to an additional aggregate principal amount not to exceed $5.0 million, at any time on or prior to December 31, 2022, upon the achievement of all of the following milestones, inclusively: (a) positive Phase 2 clinical activity data from the Company's CAN-2409 NSCLC clinical trial, (b) dosing of its first patient in its Phase 3 CAN-2409 high-grade glioma clinical trial; and (c) receipt on or prior to December 31, 2022, of net cash proceeds in an amount equal to at least $75.0 million from the issuance and sale of equity securities to investors acceptable to SVB. The Company did not borrow any of the additional aggregate principal amount on or prior to December 31, 2022. The term loan is secured by substantially all of the Company's properties, rights and assets, except for its intellectual property, which is subject to a negative pledge under the Loan Agreement.

The term loans bear interest at a floating rate per annum equal to the greater of (A) 5.75% and (B) the prime rate (as published in the money rates section of The Wall Street Journal) plus 2.50%. The Company is required to make monthly interest payments, and commencing on February 1, 2024, 24 consecutive installments of principal plus monthly payments of accrued interest. The term loans mature on January 1, 2026. Upon repayment in full of the term loans, the Company will be required to pay a final payment fee equal to 4.50% of the original principal amount of any funded term loan being repaid. The Loan Agreement permits voluntary prepayment of all, but not less than all, of the SVB term loans, subject to a prepayment premium of 1% to 3% based upon the timing of the repayment.

During the year ended December 31, 2022 , the Company recorded interest expense relating to the Loan Agreement of $1.6 million . The weighted average effective interest rate as of December 31, 2022 was 9.54%.

The Company incurred $89,000 of debt issuance costs and will incur a $0.9 million final payment fee, which were recorded as debt discount and are being amortized over the term of the Loan Agreement. The scheduled principal payments and net carrying amount of the term loan are as follows (in thousands):

| YEAR ENDING DECEMBER 31, | |
|---|---|
| 2023 | $ — |
| 2024 | 8,870 |
| 2025 | 10,232 |
| 2026 | 898 |
| Total principal | 20,000 |
| Final payment fee | 900 |
| Less: debt discount | (989) |
| Accretion of debt discount | 291 |
| Net carrying amount | $ 20,202 |

The carrying amount of the Company's term loan approximates fair value.

**7. Other Long-term Debt**

***Periphagen Note***

On December 9, 2019, the Company entered into a series of asset purchase agreements with Periphagen, Inc., a biopharmaceutical company focused on the development of gene therapy vectors. Under the terms of the asset purchase agreements, the Company assumed a $1.0 million promissory note bearing a contractual interest rate of 2% compounded annually, with the outstanding balance and accrued interest due upon maturity in November 2027, with no interim installments due. The estimated market rate for the Company for an unsecured loan with a maturity in November 2027 was determined to be 15.83%. Although the Company does not have a public credit rating, management estimates a CCC credit rating based on the Company's financial position and stage of development. Using the commensurate rate for a CCC rated company and based on the amount due at maturity, the present value of the future cash outflow was determined to be $0.4 million at the transaction date. As of December 31, 2022, the carrying value of the note is $0.6 million.

**8. Lease**

On February 4, 2019, the Company signed a lease agreement for its new corporate headquarters at 117 Kendrick Street in Needham, Massachusetts. The facility consists of a 15,197 square foot property which houses the corporate, clinical, laboratory and manufacturing operations for the Company. The lease term ends on August 31, 2026. Prior to occupying the new space, the Company had construction performed to modify the space to meet its needs. The Company received $0.8 million as a reimbursement by our landlord for a tenant improvement. The $0.8 million lease incentive was recorded as reduction to the lease right of use asset recorded to the Company's consolidated balance sheet upon adoption of ASC 842 on January 1, 2022.

***Disclosures under ASC 842***

For the year ended December 31, 2022, the Company has recorded $0.4 million of operating lease cost and $0.1 million of variable lease cost. The total lease expense for the year ended December 31, 2022 was $0.5 million.

Cash paid for amounts included in the lease liability for the year ended December 31, 2022 was $0.6 million.

| Other Information | DECEMBER 31, 2022 |
|---|---|
| Operating cash flows used for operating leases (in thousands) | $ 567 |
| Weighted-average remaining lease term (years) | 3.7 |
| Weighted-average incremental borrowing rate | 7.02% |

The future lease payments under non-cancelable leases at December 31, 2022, are as follows (in thousands):

| | | |
|---|---|---|
| 2023 | $ | 583 |
| 2024 | | 598 |
| 2025 | | 613 |
| 2026 | | 415 |
| Total future lease payments | | 2,209 |
| Less: imputed interest | | (259) |
| Total lease liability | $ | 1,950 |

***Disclosures under ASC 842***

For the year ended December 31, 2021, the Company recorded rent expense of $0.5 million.

The following table summarizes the future minimum lease payments due under the Company's facility lease as of December 31, 2021, presented in accordance with ASC 840, the relevant accounting standard at that time (in thousands):

| | | |
|---|---|---|
| 2022 | $ | 567 |
| 2023 | | 583 |
| 2024 | | 598 |
| 2025 | | 613 |
| Thereafter | | 415 |
| Total minimum lease payments | $ | 2,776 |

**9. Common Stock and Preferred Stock**

***Preferred Stock***

The Company has authorized 10,000,000 shares of $0.01 par value preferred stock at December 31, 2022 and 2021.

***Common Stock***

The Company has authorized 150,000,000 shares of $0.01 par value common stock at December 31, 2022 and 2021 of which 29,042,418 and 28,689,842 were issued as of December 31, 2022 and 2021, respectively. The Company had 28,919,810 and 28,689,842 outstanding shares as of December 31, 2022 and 2021, respectively. Common shares are voting and dividends may be paid when, as and if declared by the board of directors.

***Common Stock Reserved***

The Company has reserved the following shares of common stock for future issuance as of:

| | DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Stock options outstanding | 5,645,420 | 4,783,333 |
| Unvested restricted stock | 612,366 | — |
| Shares available for future grant under stock option plan | 1,311,915 | 1,878,997 |
| Warrants | 7,507,708 | 7,507,708 |
| | 15,077,409 | 14,170,038 |

***Reverse Stock Split***

In connection with the Company's IPO, on July 14, 2021, the Company’s board of directors and stockholders approved a one-for-2.4579 reverse stock split of the Company’s issued and outstanding common stock and a proportional adjustment to the existing conversion ratios for the outstanding shares of convertible preferred stock which became effective on July 15, 2021. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect the reverse stock split.

***Initial Public Offering***

The Company completed its IPO on July 29, 2021 and issued 9,000,000 shares of its common stock at a price to the public of $8.00 per share. On August 13, 2021, the Company issued an additional 887,994 shares of its common stock

at $8.00 per share pursuant to a partial exercise of the underwriters' purchase option. Total net proceeds to the Company from the issuance of the 9,877,994 shares of common stock were $71.3 million, after deducting underwriting discounts and commissions and offering expenses. Upon closing of the IPO, all outstanding shares of the Company's Preferred Stock automatically converted into 7,066,398 shares of common stock.

***Shelf Registration and At-the-Market Offerings***

On August 5, 2022, the Company filed a shelf registration statement on Form S-3 (the Shelf) with the SEC, which covers the offering, issuance, and sale by us of up to an aggregate of $200.0 million of our common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. We simultaneously entered into a sales agreement with Jefferies LLC, as sales agent, to provide for the issuance and sale by us of up to $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf (the ATM Program). The Shelf was declared effective by the SEC on August 12, 2022. As of the date hereof, no sales have been made pursuant to the ATM Program.

**10. Warrants**

The Company has the following warrants outstanding for the purchase of common stock as of December 31, 2022 and 2021:

| WARRANTS | SHARES OF COMMON STOCK SUBJECT TO WARRANTS | EXERCISE PRICE PER SHARE | EXPIRATION DATES |
|---|---|---|---|
| Series B Warrants | 3,672,484 | $ 6.81 | November 2025 |
| Conditional Series B Warrants | 3,672,484 | $ 6.81 | November 2025 |
| NC Ohio Trust | 162,740 | $ 1.46 | March 2029 |

***Series A Warrants***

Series A Warrants were issued in connection with the Series A Preferred Stock in 2016. In 2018, upon the conversion of the Series A Preferred Stock into common stock, the Series A Warrants became exercisable for common stock at an exercise price of $5.67 per share. Subsequent to the IPO, 75,946 Series A Warrants were exercised and the remaining 48,850 Series A Warrants expired in August 2021.

***Series B Warrants***

In connection with the November 13, 2018 issuance of Series B convertible preferred stock (the Series B Preferred), the Company issued to the purchaser of the Series B Preferred warrants to purchase 3,672,484 shares of common stock for $6.81 per share (the Series B Warrants), which became fully exercisable upon issuance. The Series B Warrants contain provisions allowing cashless exercise.

In addition, the Company issued to the same stockholder additional five-year warrants for the purchase of 3,672,484 shares of common stock for $6.81 per share (the Conditional Series B Warrants), which become exercisable in the event that the Company completes a future financing that meets certain financial milestones or achieves certain share prices as follows:

- 918,121 shares vest upon (1) a financing event effected through the sale of our equity securities to third parties resulting in at least $20,000,000 in gross proceeds with a per share price of $12.47, or (2) an average market price (determined over a consecutive 10-day period) of $12.47 per share;
- an additional 918,121 shares vest upon (1) a financing event with a price per share of $13.20, or (2) an average market price (determined over a consecutive 10-day period) of, $13.20 per share;
- an additional 918,121 shares vest upon (1) a financing event with a per share price of $13.94, or (2) an average market price (determined over a consecutive 10-day period) of, $13.94 per share; and
- an additional 918,121 shares vest upon (1) a financing event with a per share price of $14.68, or (2) an average market price (determined over a consecutive 10-day period) of, $14.68 per share.

On June 24, 2021, the Company's board of directors approved and on July 14, 2021 the stockholders approved, effective upon the closing of the IPO, an amendment to the terms of the Series B Warrants and the Conditional Series B Warrants to extend the expiration date from November 2023 to November 2025. In addition, the exercise period for the Conditional Series B Warrants was amended such that in the event the future financing milestones or certain share price targets described above are achieved, the Conditional Series B Warrants can only be exercised in conjunction

with the sale of the Company, on a cash or cashless exercise basis, or otherwise in November 2025 through a cashless exercise.

The Company recorded the Series B Warrants as a component of stockholder's equity at the time of issuance at their estimated fair value of $2.1 million and recorded the Conditional Series B Warrants as a liability on the consolidated balance sheet as the number of shares used to calculate the settlement is not a fixed number of shares. The Conditional Series B Warrants are remeasured to their fair value at each reporting date with changes in the fair value recognized as a component of other income (expense), net in the consolidated statements of operations. The Company will continue to recognize changes in the fair value of the Conditional Series B Warrants until each Conditional Series B Warrant is exercised, expires or qualifies for equity classification. The warrant liability fair value was $1.9 million and $18.3 million as of December 31, 2022 and 2021, respectively.

***NC Ohio Trust Warrants***

On March 20, 2019, the Company established the NC Incorporated Ohio Trust, an irrevocable trust funded by the Company. The beneficiary in the trust agreement has provided past services to the Company for more than 15 years and is a non-employee. The warrant provides the beneficiary the right to purchase 162,740 shares of the Company's common stock, $0.01 par value at an exercise price of $1.46 per share, subject to adjustments as specified in the warrant agreement. The Company recognizes the warrants as compensation expense within the consolidated statement of operations when the warrants are granted or at the service inception date if the service inception date precedes the grant date. In the period in which the grant date occurs, cumulative compensation cost shall be adjusted to reflect the cumulative effect of measuring compensation cost based on the fair value at the grant date rather than the fair value previously used at the service inception date or subsequent reporting dates. As of December 31, 2022 and 2021, a grant date was not established as there was not a mutual understanding of key terms. The Company remeasures the fair value of the award at each reporting date, as the service date preceded the grant date. The value of the warrants for 162,740 shares of common stock was $0.2 million and $1.1 million as of December 31, 2022 and 2021, respectively, and changes in the fair values were recorded as stock compensation expense within research and development expense and a credit to stockholders' equity in the consolidated financial statements.

**11. Stock Options, Restricted Stock and Stock-Based Compensation**

***Equity Incentive Plans***

The Company's 2015 Stock Plan, as amended, (the 2015 Plan) provides for the Company to sell or issue common shares or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, members of the board of directors and consultants of the Company. The 2015 Plan is administered by the board of directors and exercise prices, vesting and other restrictions are determined at its discretion. All stock option grants are non-statutory stock options except option grants to employees intended to qualify as incentive stock options under the Internal Revenue Code of 1986, as amended. Incentive stock options may not be granted at less than the fair market value of the Company's common stock on the date of grant, as determined in good faith by the board of directors at its sole discretion. Nonqualified stock options may be granted at an exercise price established by the board of directors at its sole discretion and the vesting periods may vary. Vesting periods are generally four years and are determined by the board of directors. Stock options become exercisable as they vest. Options granted under the 2015 Plan expire no more than ten years from the date of grant. As of December 31, 2022, there are no shares available for grants under the 2015 Plan and the 2015 Plan continues to govern the terms and conditions of the outstanding awards under the 2015 Plan.

On July 14, 2021, the Company's 2021 Equity Incentive Plan (the 2021 Plan) was approved by the Company's stockholders, and became effective upon completion of the IPO and serves as the successor to the 2015 Plan. 3,201,594 shares of common stock are reserved under the 2021 Plan, of which 1,311,915 shares remain available for future grants as of December 31, 2022.

***Stock Options***

Stock option activity is summarized as follows:

| | NUMBER OF STOCK OPTIONS | WEIGHTED-AVERAGE EXERCISE PRICE | WEIGHTED-AVERAGE REMAINING CONTRACTUAL TERM (IN YEARS) | AGGREGATE INTRINSIC VALUE |
|---|---|---|---|---|
| Outstanding as of December 31, 2021 | 4,783,333 | $ 2.34 | | |
| Granted | 1,873,340 | 3.92 | | |
| Exercised | (352,576) | 1.47 | | |
| Cancelled or forfeited | (658,677) | 3.48 | | |
| Outstanding as of December 31, 2022 | 5,645,420 | $ 2.77 | 7.73 | $ 881 |
| Exercisable as of December 31, 2022 | 2,876,293 | $ 2.30 | 6.86 | $ 606 |
| Unvested as of December 31, 2022 | 2,769,127 | $ 3.27 | 8.63 | $ 275 |

The 2015 Plan permits participants to use common stock they previously acquired to pay for the exercise of stock options based upon the fair value on the date of exercise. In connection with the exercise of a stock options to purchase 306,518 shares of our common stock at an exercise price of $1.46, option holders tendered 122,608 shares of our common stock previously acquired in consideration of the full aggregate exercise price in accordance with the terms of the option and the 2015 Plan. The shares tendered are recorded as treasury stock within the Company's consolidated financial statements at December 31, 2022.

The fair value of stock options granted was estimated on the grant date using the Black-Scholes option pricing model based on the following weighted-average assumptions:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Expected option life (years) | 5.33 - 6.08 | 5.00 - 10.00 |
| Risk-free interest rate | 1.69% - 4.23% | 0.89% - 1.35% |
| Expected volatility | 85.09% - 87.67% | 83.80% - 89.02% |
| Expected dividend yield | 0 % | 0 % |
| Exercise price | $1.75 - $5.19 | $4.97 - $11.23 |
| Fair value of common stock | $1.75 - $5.19 | $4.97 - $11.23 |

The total intrinsic value of stock options vested during the years ended December 31, 2022 and 2021 was zero and $6.6 million, respectively.

***Restricted Stock***

Under the terms of the restricted stock unit agreements covering the common stock, shares of common stock related to restricted stock units are subject to time-based and performance-based vesting. The restricted stock units will immediately be forfeited to the Company if the relationship between the recipient and the Company ceases.

Restricted stock activity is summarized as follows:

| | NUMBER OF SHARES OPTIONS | WEIGHTED-AVERAGE GRANT DATE FAIR VALUE |
|---|---|---|
| Unvested at December 31, 2021 | — | $ — |
| Granted | 612,366 | $ 1.71 |
| Vested | — | $ — |
| Forfeited | — | $ — |
| Unvested at December 31, 2022 | 612,366 | $ 1.71 |

The aggregate fair value of restricted stock units that vested during each of the years ended December 31, 2022 and 2021 was zero.

***Stock-Based Compensation***

Stock-based compensation expense for the years ended December 31, 2022 and 2021 was classified in the consolidated statements of operations as follows (in thousands):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Research and development | $ 774 | $ 1,226 |
| General and administrative | 1,533 | 1,737 |
| Total stock based compensation expense | $ 2,307 | $ 2,963 |

As of December 31, 2022 and 2021, total unrecognized compensation cost related to the unvested stock-based awards was $7.6 million and $6.3 million, respectively. As of December 31, 2022 and 2021, these amounts are expected to be recognized over a weighted average period of 2.42 and 2.26 years, respectively.

**12. Income Taxes**

Due to the Company's net losses for 2022 and 2021, as well as the full valuation allowance on its net deferred tax assets as discussed below, the Company did not record any income tax expense or benefit for the years ended December 31, 2022 and 2021.

A reconciliation of income tax expense at the federal statutory income tax rate to the income tax expense at the Company's effective income tax rate is as follows:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Income at US statutory rate | 21.00 % | 21.00 % |
| Permanent adjustments | (2.84 )% | (0.59 )% |
| Mark to market | 18.29 % | (6.64 )% |
| State taxes, net of federal benefit | 12.78 % | 4.01 % |
| Valuation allowance | (56.79 )% | (19.86 )% |
| Tax credits | 7.56 % | 2.08 % |
| | — | — |

Net deferred tax assets as of December 31, 2022 and 2021 consist of the following (in thousands):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Deferred tax assets: | | |
| Net operating losses | $ 17,748 | $ 13,892 |
| Intangibles | 572 | 654 |
| Accrued expenses and other | 601 | 243 |
| Deferred revenue | — | 34 |
| Lease liability | 524 | — |
| Stock Compensation | 863 | 820 |
| Capitalized R&D expenditures | 4,931 | — |
| Credits | 4,755 | 2,850 |
| Total deferred tax assets | 29,994 | 18,493 |
| Valuation allowance | (29,166 ) | (18,493 ) |
| Deferred tax assets | 828 | — |
| Deferred tax liabilities: | | |
| Right of use asset | (284 ) | — |
| Other | (544 ) | — |
| Total deferred tax liabilities | (828 ) | — |
| Net deferred tax assets (liabilities) | $ — | $ — |

As of December 31, 2022, the Company has gross federal and state net operating loss carryforwards of approximately $65.9 million and $61.9 million which begin to expire in 2027 and 2032, respectively. Additionally, the Company has $57.1 million of the federal net operating loss carryforwards that can be carried forward indefinitely.

As of December 31, 2022, the Company has gross federal and state tax credit carryforwards of approximately $3.4 million and $1.8 million, respectively, which begin to expire in 2036 and 2028, respectively.

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of net operating loss carryforwards and certain tax credits. Management has considered the Company's history of cumulative net losses incurred since inception, as well as its lack of product revenue since inception, and has determined that it is more likely than not that the Company will not realize the benefits of its deferred tax assets. As a result, a full valuation allowance has been established at December 31, 2022 and 2021.

Section 382 of the Internal Revenue Code of 1986, as amended ("Section 382"), contains rules that limit the ability of a company that undergoes in ownership change to utilize its net operating losses ("NOLs") and tax credits existing as of the date of such ownership change. Under the rules, such an ownership change is generally any change in ownership of more than 50% of a company's stock within a rolling three-year period. The rules generally operate by focusing on changes in ownership of all stock considered by the rules as owning, directly or indirectly, 5% or more of the stock of a company and any change in ownership arising from new issuances of stock by the company. The Company has not yet determined if such a limitation would be placed against its available net operating losses. The Company will make such a determination prior to the utilization of any future net operating losses.

A summary of changes in the valuation allowance for deferred tax assets during the year ended December 31, 2022 and 2021 were as follows (in thousands):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Valuation allowance | $ 18,493 | $ 11,318 |
| Increases recorded to income tax provision | 10,673 | 7,175 |
| Decreases recorded to income tax provision | — | — |
| Valuation allowance | $ 29,166 | $ 18,493 |

The Company files income tax returns in the United States and various state and local jurisdictions. The federal and state tax returns are generally subject to examination for the years ended December 31, 2014 through December 31, 2022. There are currently no pending tax examinations. To the extent the Company has tax attribute carryforwards, the tax year in which the attribute was generated may still be adjusted upon examination.

**13. Exclusive Licensing Agreement with a Related Party**

In March 2014, the Company entered into an exclusive licensing agreement with Ventagen, LLC (Ventagen) which provides Ventagen the right to develop products for commercial sale and distribution within Mexico, Belize, Guatemala, Honduras, El Salvador, Costa Rica, Nicaragua, Panama, Colombia, and Bolivia (the Territory). Ventagen paid the Company $1.0 million upon the signing of the agreement and agreed to a fixed future payment to the Company of $2.5 million. The future payment will be made upon the achievement of $5.0 million of sales of an approved product by Ventagen and is subject to reduction if Ventagen's costs to develop an approved product exceeds $4.0 million. In addition to the upfront payment and the future payment, Ventagen agreed to purchase from the Company all manufactured product that is required for clinical or commercial purposes at a price of cost plus 25% of the wholesale price of the approved product subject to a minimum or maximum price. In the event the Company is unable or unwilling to manufacture supply under the terms of the agreement, Ventagen has the right to manufacture its own supply and will be required to pay a fixed fee per dose sold. The Company also agreed to provide certain services to Ventagen related to Ventagen's development plan. Stockholders of the Company own 49.5% of the voting stock of Ventagen, including 47% by the Company's founders who are currently significant stockholders of the Company, and trusts for the benefit of their children.

The Company is recognizing the $1.0 million upfront license fee as research and development service revenue, related party, as the Company's license agreement with Ventagen is within the scope of ASC 606. The license agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. The terms of the agreement contained multiple, distinct performance obligations, including transfer of a license for the Territory, research and development oversight for the trials run by Ventagen, and clinical data sharing.

The Company estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations. The performance obligation associated with the license transfer was satisfied at a point in time, or at contract inception; however, the Company assigned no value to the license transfer. The remaining $1.0 million transaction price was allocated between the research and development oversight and clinical data sharing. The Company is recognizing revenue for these obligations over an 8-year period, beginning in 2015, by measuring the progress towards satisfaction of the performance obligations. As clinical oversight and clinical

data sharing occurs over the 8—year clinical trial period, the revenue is recognized over the same period in which the cost for these services is incurred.

The Company defers recognition of the portion of the $1.0 million non-refundable upfront license fee for the portion of the performance obligations that are not satisfied. The Company recognized revenue of $0.1 million in the years ended December 31, 2022 and 2021. The license agreement includes a $2.5 million potential future milestone payment due to the Company upon successful completion of certain separate, distinct events. At this time, the Company cannot estimate when the milestone-related performance obligations are expected to be achieved and will recognize revenue once satisfaction is probable. There was no additional variable consideration, significant financing components, non-cash consideration, or consideration payable to the customer in this agreement.

**14. Technology License Agreement**

On January 20, 2018 the Company entered into an exclusive option agreement (Option Agreement) with MGB. Pursuant to the Option Agreement, the Company has obtained the exclusive right from MGB to negotiate an exclusive license to make, develop and commercialize rQNestin, a genetically modified oncolytic herpes simplex virus for the treatment of certain types of cancers. Pursuant to the Option Agreement, the Company will support a clinical trial to be conducted at MGB pursuant to the terms of a clinical trial agreement to be negotiated and the Company has committed to remitting $0.8 million in support of such clinical trial over the course of approximately three years. Upon execution of the Option Agreement, the Company remitted a non-refundable fee of $40,000 to MGB to be applied toward the Company's on-going obligations to reimburse patent expenses. In the years ended December 31, 2022 and 2021, respectively, the Company expensed zero and $28,000, respectively, for startup and patient fees for clinical trials performed by MGB.

On September 15, 2020, the Company exercised the Option Agreement with MGB and entered into an exclusive worldwide patent license agreement with MGB (the MGB License). In connection with the MGB License, the Company paid a fee of $0.1 million and agreed to reimburse patent costs incurred by MGB, including $0.1 million paid at the time of entering into the MGB License. Prior to the first commercial sale, the Company is required to pay MGB an annual license fee of $50,000 beginning following the fourth anniversary of the effective date. The MGB License contains cumulative milestone payments equaling a maximum amount of $39.0 million upon the achievement of various clinical, commercial and sales milestones of both primary and secondary products. Following the first commercial sale, the Company is required to pay royalties to MGB, which are paid at an increasing rate as net sales increase, ranging from low single digits to high single digits. In addition, after the first commercial sale, the Company is required to pay MGB a pre-determined fixed annual minimum royalty, which amount may be credited against earned royalties starting in the fourth year following the first commercial sale. The Company also agreed to pay a single digit royalty rate on net sales of any derived products.

**15. Commitments and Contingencies**

***Guarantees***

The Company has identified the guarantees described below as disclosable, in accordance with ASC 460, Guarantees.

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that should limit its exposure and enable it to recover a portion of any future amounts paid.

The Company is a party to a number of agreements entered into in the ordinary course of business that contain typical provisions that obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain.

The Company leases office space under a noncancelable operating lease expiring in 2026. The Company has standard indemnification arrangements under this lease that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the lease.

As of December 31, 2022, the Company had not experienced any losses related to these indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves have been established.

***Legal Proceedings***

From time to time, we may become involved in litigation or other legal proceedings. On December 15, 2022, Periphagen notified us by letter of its claim that we have failed to use commercially reasonable efforts to complete a human proof of concept clinical trial of an NT-3 Asset under an Exclusive License Agreement dated December 9, 2019 between us and Periphagen (the "Periphagen License Agreement"). We have denied Periphagen's claims. On January 13, 2023, we filed a demand for arbitration against Periphagen with the American Arbitration Association, seeking a declaration that Periphagen's December 15 letter failed to comply with the dispute and escalation provisions in the Periphagen License Agreement. After filing the demand, the parties began engaging in the dispute and escalation process under the Periphagen License Agreement. On March 10, 2023, Periphagen filed its answer and counterclaims to our demand for arbitration. In its counterclaims, Periphagen seeks a declaration that we have not used commercially reasonable efforts to complete a human proof of concept clinical trial of the NT-3 Asset and a declaration that any further extension of time would not be scientifically or commercially reasonable. Periphagen also seeks a declaration that Candel must use commercially reasonable efforts to develop the NT-3 Asset during any remaining time under the agreement. We have denied Periphagen's counterclaims.

In the event the parties are unable to resolve the dispute as part of the escalation process, an arbitrator will decide whether we have used commercially reasonable efforts. In the event that the arbitrator determines that we have not used commercially reasonable efforts, then we may submit a specified payment in lieu of satisfying such obligations.

Aside from the proceeding with Periphagen, we are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

**16. Net Loss Per Share**

***Net Loss Per Share***

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share data):

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| **Numerator:** | | |
| Net loss | $ (18,794) | $ (36,124) |
| **Denominator:** | | |
| Weighted-average shares of common stock outstanding-basic and diluted | 28,823,480 | 18,873,048 |
| Net loss per share -basic and diluted | $ (0.65) | $ (1.91) |

The Company's potentially dilutive securities have been excluded from the computation of dilutive net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share is the same.

The Company excluded the following potential shares of common stock from the computation of diluted net loss per share because including them would have had an anti-dilutive effect.

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2022 | 2021 |
| Outstanding warrants for common stock | 7,507,708 | 7,507,708 |
| Outstanding stock options (as converted to common stock) | 5,645,420 | 4,783,333 |
| Unvested restricted stock | 612,366 | — |
| | 13,765,494 | 12,291,041 |

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Candel Therapeutics, Inc.

Date: March 30, 2023

By: /s/ Paul Peter Tak

**Paul Peter Tak, M.D., Ph.D., FMedSci**
**President and Chief Executive Officer**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

| Name | Title | Date |
|---|---|---|
| /s/ Paul Peter Tak<br>**Paul Peter Tak, M.D., Ph.D. FMedSci** | President and Chief Executive Officer (Principal Executive Officer) | March 30, 2023 |
| /s/ Jason A. Amello<br>**Jason A. Amello** | Chief Financial Officer (Principal Financial and Accounting Officer) | March 30, 2023 |
| /s/ Paul B Manning<br>**Paul B Manning** | Chairman | March 30, 2023 |
| /s/ Edward J. Benz Jr.<br>**Edward J. Benz, Jr, M.D.** | Director | March 30, 2023 |
| /s/ Chris Martell<br>**Chris Martell** | Director | March 30, 2023 |
| /s/ Renee Gaeta<br>**Renee Gaeta** | Director | March 30, 2023 |
| /s/ Gary Nabel<br>**Gary Nabel, Ph.D., M.D.** | Director | March 30, 2023 |
| /s/ Estuardo Aguilar-Cordova<br>**Estuardo Aguilar-Cordova, M.D. Ph.D.** | Director | March 30, 2023 |
| /s/ Joseph Papa<br>**Joseph Papa** | Director | March 30, 2023 |
| /s/ Diem Nguyen<br>**Diem Nguyen, Ph.D., MBA** | Director | March 30, 2023 |

**CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF DISCLOSED.**

# MASTER PRODUCTION SERVICES AGREEMENT

THIS MASTER PRODUCTION SERVICES AGREEMENT, entered into and effective November 3, 2022 (the "Effective Date"), is by and between SAFC CARLSBAD, INC., a California corporation located at 6211 El Camino Real, Carlsbad, CA 92009 ("PROVIDER"), and Candel Therapeutics, Inc., a Delaware corporation located at 117 Kendrick St., Suite 450, Needham, MA 02494 ("CLIENT"). PROVIDER and CLIENT may be referred to individually as "party" and collectively as "parties".

WHEREAS, CLIENT desires that PROVIDER or its Affiliates, as applicable, conduct certain development, production, manufacturing, and/or contract testing services from time to time during the term of this Agreement; and

WHEREAS, PROVIDER and CLIENT desire to establish initially herein general terms and conditions governing the conduct of such services;

WHEREAS, prior to the Effective Date, the parties entered into a Manufacturability and Gap Assessment and related Terms and Conditions (collectively, the "MGA") to authorize PROVIDER to commence providing certain preliminary Services while this Master Production Services Agreement was being negotiated and executed.

NOW, THEREFORE, in consideration of the mutual covenants and agreements contained herein, the parties hereto agree as follows:

## ARTICLE 1 - DEFINITIONS

As used herein, the following capitalized terms shall have the meanings set forth below:

1.1. "Affiliate(s)" means any legal entity that directly or indirectly controls, is controlled by, or is under common control with a party, for as long as such control exists. "Control", "controlled by" and "under common control" as used in this definition refers (a) to the ownership, directly or indirectly, of more than [***] of the outstanding voting securities or the capital stock of, or other comparable equity or ownership interest in the respective legal entity, or (b) in the absence of such ownership interest, to the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of the respective legal entity, by contract or otherwise.

1.2. "Agency" means (a) any regulatory or health authority in the US or in other countries, including the US Food and Drug Administration or any successor entity thereto ("FDA") and the European Medicines Agency or any successor entity thereto, and (b) if applicable to a particular Task Order, the relevant government regulatory authority or authorities in countries outside of the United States responsible for the conduct of clinical research studies and/or approval of pharmaceutical products necessary for the manufacture, marketing, importation and sale of such pharmaceutical products and, to the extent required in such country or regulatory jurisdiction, pricing or reimbursement approval of such pharmaceutical products in such country or regulatory jurisdiction.

1.3. "Agreement" means, collectively, this Master Production Services Agreement, its Exhibits, any Task Orders and any other documents incorporated herein by reference, including the Quality Agreement(s).

1.4. "Batch" means a specific quantity of Drug Substance or Drug Product, as applicable in the given context, that is intended to have uniform character and quality within specified limits and is produced according to a single cycle of Manufacture and may be comprised of multiple Batch Records.

1.5. "Batch Record" (also sometimes referred to as "Manufacturing Batch Record" ("MBR") or "Batch Production Record" ("BPR")) means a Manufacturing record for a Batch generated by PROVIDER concurrently with the production of a specific Batch such that successive steps in such processes, including methods, are documented.

1.6. "Business Partners" means any entity which is not an Affiliate of CLIENT and that has a business relationship or collaboration with CLIENT or its Affiliates.

1.7. "cGLP" means the then-current standards for laboratory activities for pharmaceuticals, as are required by Agencies, including the regulatory authorities of Europe, the United States and Japan, including 21 C.F.R. part 58, 21 CFR 320.29, and EC Directives 87/18/EEC, 88/320/EEC and 1999/11/EC, in each case, as amended from time to time and any relevant international standards or principles such as those adopted by the Organization for Economic Co-operation and Development.

1.8. "cGMP" shall mean then current good manufacturing practices pursuant to (a) the FDC Act, (b) U.S. regulations in Title 21 of the U.S. Code of Federal Laws Parts 210, 211, 600 and 610, (c) the EC Guide to Good Manufacturing Practice for Medicinal Products, v.4, including relevant sections of DIR 2003/94/EC, and (d) International Conference on Harmonization (ICH) Guidance for Industry Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, in each case as in effect and as may be amended or replaced from time to time.

1.9. "Certificate of [***]" means the certificate issued by [***].

1.10. "Certificate of [***]" means the certificate issued by [***].

1.11. "CFR" means the U.S. Code of Federal Laws.

1.12. "CLIENT Equipment" means Project Equipment that is specified in the Task Order as to be supplied by CLIENT or that CLIENT requires PROVIDER to obtain for the Project (at CLIENT'S cost).

1.13. "CLIENT Materials" means those Project Materials that are specified in the Task Order as being supplied by CLIENT, or that CLIENT requires PROVIDER to obtain for the Project pursuant to Section 2.2(a) or Section 4.4.

1.14. "CLIENT Technology" means information and know-how, techniques, processes, and other technology, whether or not patentable or copyrightable, and associated intellectual property that CLIENT or its Affiliates owns or has rights to, and is provided to PROVIDER to perform the Services. CLIENT Technology includes manufacturing methods, Specifications, the packaging components, the CMC, the production monograph, the Master Batch Records and testing methods that have been disclosed by, or on behalf of, CLIENT or its Affiliates to PROVIDER or its Affiliates under the terms of this Agreement or before the execution of this Agreement pursuant to any confidentiality agreement, feasibility study agreement, manufacturing agreement, or will be disclosed to PROVIDER or to its Affiliate after the execution of this Agreement, or are developed by, or on

behalf of PROVIDER or its Affiliates for CLIENT or its Affiliates. CLIENT Technology also includes all CLIENT Inventions.

1.15. "CMC" means the chemistry, manufacturing, and controls section(s) and data in any Health Registration(s) that covers the chemical composition of a given Product and its components and the control and Manufacturing process for any Products and their components, including the Drug Substance or Drug Product, as may be amended or supplemented from time to time.

1.16. "Confidential Information" means CLIENT Confidential Information and/or PROVIDER Confidential Information, as the case may be.

1.17. "Convicted Entity" means an entity who has been convicted of a criminal offense that falls within the ambit of 21 U.S.C. §1320a - 7(a) or otherwise convicted under the corresponding Law of another jurisdiction, but has not yet been excluded, debarred, suspended or otherwise declared ineligible.

1.18. "Convicted Individual" means an individual who has been convicted of a criminal offense that falls within the ambit of 21 U.S.C. §1320a - 7(a) or otherwise convicted under the corresponding Law of another jurisdiction, but has not yet been excluded, debarred, suspended or otherwise declared ineligible.

1.19. "Debarred Entity" means a corporation, partnership, entity or association that has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) or otherwise debarred under the corresponding Law of another jurisdiction from submitting or assisting in the submission of any abbreviated drug application, or a subsidiary or Affiliate of a Debarred Entity.

1.20. "Debarred Individual" means an individual who has been debarred by the FDA pursuant to 21 U.S.C. §335 (a) or (b) or otherwise debarred under the corresponding Law of another jurisdiction from providing services in any capacity to a person that has an approved or pending drug product application.

1.21. "Deliverables" means the item (interim and/or final), including any applicable data, records, and reports, to be provided by PROVIDER to CLIENT as part of a Task Order, and to be delivered to CLIENT, all in accordance with the relevant Task Order and this Agreement, and which may include Drug Product, Drug Substance or Product .

1.22. "Drug Substance" means, with respect to a given Product, the bulk intermediate or active pharmaceutical ingredient identified in the applicable Task Order.

1.23. "Drug Product" means, with respect to a given Product, the final drug product for such Product, in its final container closure, whether or not labeled, and identified in the applicable Task Order.

1.24. "Effective Date" means, for this Master Production Services Agreement, the date set forth in the preamble of this Master Production Services Agreement, and for each Project defined in a Task Order, the date specified as the "Effective Date" or the like in said Task Order.

1.25. "Excluded Entity" means (a) an entity who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal health care programs such as Medicare or Medicaid by the Office of the Inspector General ("OIG/HHS") of the Department of Health and Human Services, or (b) who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal procurement and non-procurement programs, including those produced by the United States General Services Administration ("GSA"), or otherwise excluded, debarred, suspended or is otherwise ineligible under the corresponding Law of another jurisdiction.

1.26. "Excluded Individual" means (a) an individual who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal health care programs such as Medicare or Medicaid by the OIG/HHS, or (b) who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal procurement and non-procurement programs, including those produced by the GSA, or otherwise excluded, debarred, suspended or is otherwise ineligible under the corresponding Law of another jurisdiction.

1.27. "Facility" means the PROVIDER or its Affiliate location at which any Services are being performed. Such term includes all of the equipment, machinery and facilities of the PROVIDER at such location that are used to perform the Services or in the Manufacturing and storage of such Product.

1.28. "FDC Act" means the U.S. Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§301-397, together with any regulation or guidance promulgated thereunder, in each case as amended from time to time.

1.29. "Health Registration" means the technical, medical and scientific licenses, registrations, authorizations and/or approvals of a Product that are required by any national, supra-national (*e.g.*, the European Commission or the Council of the European Union), regional, state or local Agency or other governmental entity, for the Manufacture, use or sale of the subject Product. For clarity, Health Registrations shall exclude any Permits specific to the Facility.

1.30. "Laws" means any and all laws, rules, regulations, ordinances, statutes, codes, guidelines, guidances, treaties, judgments, decrees, directives, injunctions, requirements and court orders of any kind whatsoever of any governmental entity (including any Agency) applicable to a party's activities hereunder, as amended from time to time, including cGLP, cGMP (if applicable), the ICH guidelines and regulations, the U.S Foreign Corrupt Practices Act (FCPA), and the FDC Act, governing the performance of the Services in the country or countries in which the Services are conducted or otherwise applicable to a party's performance in connection with this Agreement. Any reference to a particular law or regulation will be interpreted to include any revision of or successor to such statute, law, rule or regulation regardless of how it is numbered or classified.

1.31. "Manufacture," "Manufactured," or "Manufacturing" means any and all processes of cell banking, manufacturing and/or blending of CLIENT Materials, including compounding, component and/or intermediary preparation, production, packaging, labeling, testing, inspecting, quality control, storage, and preparing for shipment of Deliverable, which may include Product, in accordance with the Technical Specifications and other requirements of this Agreement.

1.32. "Master Batch Record" means the document, which shall be mutually agreed to by both parties, containing the Technical Specifications and instructions for the Manufacture and quality assurance of Product, as such may be amended by the parties in accordance with the terms hereof.

1.33. "Permit" means any application, accreditation, permit, authorization, license, approval, registration, franchise, certificate, permission, exemption, consent, variance (including zoning variance approval), or equivalent decision or document of, from, or required or issued by, any Agency or under any Law for the operation of the Facility or the Manufacture of Product by PROVIDER at the Facility, as amended or supplemented from time to time.

1.34. "Process Development Services" mean the conduct by PROVIDER of activities to develop, confirm and/or refine processes for producing the Deliverable and/or activities to develop and/or scale-up a Manufacturing process suitable for cGMP Manufacture of the Product. Any and all improvements to the Manufacturing process shall constitute CLIENT Technology.

1.35. "Product" means the pharmaceutical product to be Manufactured by PROVIDER as described in a given Task Order.

1.36. "Production Records" means all documentation, Records, required retain samples, Batch Records, Technical Specifications, databases or other work product generated by PROVIDER during and in connection with a Project.

1.37. "Project" means an individual clinical production or laboratory testing project for which PROVIDER is engaged by CLIENT to perform Services and "Projects" means, collectively, all such Projects.

1.38. "Project Equipment" means all equipment necessary to perform the Project and deliver the Deliverable.

1.39. "Project Initiation Date" means the date identified as such on the Task Order as the mutually agreed upon target date for initiation of the Project.

1.40. "Project Materials" means all cell banks, virus banks, compounds, materials, supplies or other substances necessary to perform the Project and deliver the Deliverable.

1.41. "PROVIDER Technology" means certain background knowledge, know how, analytical methods, personnel data, financial information, production notes, computer technical expertise and software which: (a) is independently developed by PROVIDER at any time without use of, reliance on, or reference to CLIENT Technology or CLIENT Confidential Information, including any of the foregoing which relates generally to PROVIDER'S business operations and/or scientific expertise and/or experience in the development, production, and manufacture of products and/or services; and/or (b) arises out of or relates to PROVIDER Technology without use of, reliance on, or reference to CLIENT Technology or CLIENT Confidential Information. PROVIDER Technology is wholly owned by PROVIDER. PROVIDER may utilize PROVIDER Technology to complete the Service(s) set forth in this Agreement. Except as expressly set forth herein, PROVIDER does not grant any right, title or interest in PROVIDER Technology by virtue of the instant Agreement and/or the performance of any Services in connection with this Agreement, whether or not patentable or copyrightable, and associated intellectual property. PROVIDER Technology shall in no case be deemed to include or encompass any CLIENT Technology.

1.42. "Quality Agreement" means the quality agreement which will be executed between PROVIDER and CLIENT and a quality agreement to be executed between an Affiliate of PROVIDER and CLIENT, where and when applicable, as such agreements may be amended from time to time. Quality Agreements may be amended and modified separately as stand-alone documents and shall not require an amendment of this Master Production Services Agreement.

1.43. "Records" means the written records of data and other information generated or recorded in the performance of the Services and other information related to the performance of the Services, including Master Production Records, Batch Records, Reports, test results, records of the procedures, source data, raw data, Technical Specifications, Certificates of [***], and Certificates of [***].

1.44. "Reports" means the written interim or final Project report(s) which may be required in a Task Order and/or by the Laws.

1.45. "Specification(s)" means the Technical Specification(s) and any additional non-warranted specifications for the finished Deliverable as measured by PROVIDER, PROVIDER'S Affiliate, or CLIENT'S Third Party testing lab and reported by PROVIDER, PROVIDER'S Affiliate, or CLIENT'S third party testing lab in the Certificate of [***].

1.46. "Standard Operating Procedure(s)" or "SOP(s)" means the written procedures, which shall govern the performance of the Service(s), which procedures are or may be more particularly addressed in Section 2.4.

1.47. "Task Order" means a mutually executed written description of the Service(s) to be performed by PROVIDER, pursuant to this Agreement, which describes an individual Project and the scope of work to be undertaken for such Project. In addition to the description of the Services, each Task Order will include a description of the Deliverables, CLIENT Materials, Project initiation and completion dates, timelines, Technical Specifications, fees, payment schedules, non-refundable deposit(s) and such other details and special arrangements as are agreed to by the parties. A sample form of a Task Order is attached hereto as Exhibit A.

1.48. "Technical Specification(s)" means warranted Specifications as set forth within a Task Order.

1.49. "Technical Transfer" means the project to transfer and adapt CLIENT'S current Manufacturing process for the Manufacture of Product to the Facility.

1.50. "Technical Transfer Plan" means the written plan, including deliverables and schedule, developed and agreed to in writing by the parties and set forth in a Task Order or multiple Task Orders, which may be revised and modified from time to time by mutual written agreement of the parties via a Change Order.

1.51. "Third Party" means any person or entity who or which is neither a party to this Agreement nor an Affiliate of a party.

ARTICLE 2 - GENERAL PROVISIONS.

2.1. Engagement and Commitment. CLIENT hereby engages PROVIDER on a non-exclusive basis to provide the Services set forth in this Agreement and any Task Order(s) arising from this Agreement, and PROVIDER hereby agrees to provide to CLIENT the Services, including testing and development, and Manufacturing, supply, and production of Deliverable as more particularly described in this Agreement and each individual Task Order arising from this Agreement (the "Services").

(a) This Agreement shall constitute the entire agreement between the parties with respect to each Project. To the extent any terms in a Task Order, Quality Agreement, attachment, purchase order, invoice, or any other document related to this Agreement and/or any Project conflict with the terms of this Agreement:

(i) the terms of the Quality Agreement will control with respect to quality matters,

(ii) the terms of the Task Order will control with respect to any provision that expressly states that it overrides the applicable term of this Agreement, and

(iii) the terms of this Agreement shall control for all other matters.

Any changes to Task Orders shall be made in accordance with Section 2.5 below.

(b) PROVIDER will perform Services for CLIENT using due care in accordance with, as applicable to the particular Project, (a) this Agreement, including the relevant Task Order and the Quality Agreement; (b) the Technical Specifications; and (c) applicable Laws.

(c) PROVIDER agrees to provide to CLIENT (i) all Batches of Deliverables which meet the standards defined in Section 2.1(b) of this Agreement and the warranty set forth in Section 8.3 (each a "Conforming Deliverable"), and (ii) and any other Deliverables required by this Agreement.

(d) PROVIDER shall not Manufacture or transfer, or cause to be Manufactured or transferred, the Deliverable or any Product containing the Deliverable for any purpose other than fulfilling or relating to its obligations to CLIENT hereunder.

(e) PROVIDER shall ship the Deliverables, as applicable, to CLIENT (or CLIENT'S designee) at CLIENT'S cost, FCA Shipping Point (INCOTERMS 2020). Risk of loss shall be the responsibility of CLIENT and title shall transfer to CLIENT upon release of Deliverable and/or Deliverables from PROVIDER'S premises to a qualified shipper selected by PROVIDER (unless PROVIDER otherwise expressly agrees to permit CLIENT to select the shipper at CLIENT'S risk, in which case PROVIDER shall use such shipper). All freight, storage, insurance or other costs of shipment and all taxes, duties or other fees and charges, if any, in connection with the shipment of the Deliverable shall be paid by CLIENT and, if advanced by PROVIDER, shall be added to CLIENT'S invoice and payable together with payment for the Services. In the absence of express instructions from CLIENT, PROVIDER shall not be responsible for the choice of carrier or routing of any shipment, for the scope of coverage afforded by any insurance, for the reasonableness of any freight, insurance or other charges incurred for CLIENT account or for any other matters relating to the shipment and PROVIDER shall be deemed to be authorized by CLIENT to arrange for such carriage, routing and insurance and to incur such charges as PROVIDER, in its discretion, deems reasonable under the circumstances.

2.2. Project Materials and Equipment.

(a) If CLIENT Material(s) and/or CLIENT Equipment are required for the performance of the Services, CLIENT shall provide PROVIDER with sufficient quantities of such CLIENT Materials and CLIENT Equipment as set forth in the applicable Task Order necessary to perform the Services, including sufficient and comprehensive data as may be required by PROVIDER concerning handling, stability, storage and safety requirements of CLIENT Materials and CLIENT Equipment, as well as any other information which CLIENT reasonably believes would be helpful to PROVIDER in the performance of the applicable Services. If CLIENT requires PROVIDER to acquire special Project Materials or Project Equipment, such materials and equipment shall be considered CLIENT Materials and CLIENT Equipment, and shall be charged to the account of CLIENT on a pass through basis, plus any applicable handling or service fee specifically set forth in the applicable Task Order, and CLIENT shall at all times be fully responsible (i) for all costs, expenses, maintenance, and other issues in connection with such CLIENT Materials and/or CLIENT Equipment, as explicitly set forth in the applicable Task Order, as well as (ii) for all bear risk of loss and/or damage to such CLIENT Materials and CLIENT Equipment (other than any damage or loss caused by PROVIDER'S gross negligence or intentional misconduct, or that of any subcontractor or other person or entity for which PROVIDER is responsible, which shall be the responsibility of PROVIDER).

(b) Title to CLIENT Materials and CLIENT Equipment shall remain with CLIENT. PROVIDER will not use CLIENT Materials and/or CLIENT Equipment for any purpose other than in connection with fulfilling its obligations under this Agreement, including the applicable Task Order and as part of an investigation on the CLIENT'S process. Except as may be specifically set forth in this Agreement, or any Task Order, PROVIDER will not transfer the

CLIENT Materials and/or CLIENT Equipment to any Third Party without the prior written consent of CLIENT.

(c) PROVIDER shall provide safe and secure storage conditions for CLIENT Materials and CLIENT Equipment in accordance with PROVIDER standard operating procedures while they are at the Facility and shall use commercially reasonable care and precautions to protect CLIENT Materials and CLIENT Equipment from loss, damage, or contamination during storage at the Facility.

(d) Unless otherwise specified and provided by CLIENT (or obtained at the behest of CLIENT), PROVIDER will use such Project Materials and Project Equipment that it reasonably believes are appropriate for its performance of the Services.

(e) A quarterly virtual inventory of all the CLIENT Materials, CLIENT Equipment and any material that is generated as part of the Task Orders shall be performed by the PROVIDER using PROVIDER'S validated inventory management system and shared with the CLIENT.

(f) Except as specifically agreed by the parties in writing, or unless prohibited by Laws, any remaining supplies of CLIENT Materials or any CLIENT Equipment shall be returned to CLIENT, at CLIENT'S cost, within [***] of final disposition of the Batch, unless CLIENT directs otherwise (in which case CLIENT shall be responsible for all disposal, storage, and removal costs). CLIENT will be automatically charged applicable storage fees, at no more than PROVIDER'S then standard rates for storage, for any remaining supplies of CLIENT Materials or CLIENT Equipment that are not returned to the CLIENT within [***] of final Batch disposition or if not anticipated to be used within the following [***] pursuant to the same or another Task Order.

(g) All CLIENT Equipment shall be maintained by PROVIDER per PROVIDER'S maintenance program and the applicable manufacturer requirements, at CLIENT'S cost as specified in the applicable Task Order. CLIENT Equipment shall at all times remain the property of CLIENT (and PROVIDER shall ensure that no pledges, liens, restrictions, claims, charges, security interests or other encumbrance are placed on such CLIENT Equipment, other than by CLIENT or its Affiliate).

(h) If a given Product is to be supplied hereunder in finished packaged form, then CLIENT shall, to the extent applicable to such Product, provide PROVIDER with packaging and labeling images (e.g., CLIENT trademarks and trade dress and other artwork) as and to the extent determined by CLIENT, solely for PROVIDER'S use for the packaging and labeling of such Products hereunder, including specifications related to the format and size thereof. All use of such packaging and labeling images shall be at the direction of CLIENT, and CLIENT shall have the right at any time (in its discretion) with sufficient written notice to cause PROVIDER to modify the way such packaging and labeling images are being used or otherwise cause PROVIDER to cease using such packaging images entirely. PROVIDER shall not modify such packaging and labeling images in any way. For clarity, PROVIDER shall have no rights or licenses in or to any trademarks, trade dress or other artwork with respect to such packaging and labeling images, and all rights and uses thereof (including all goodwill) shall accrue solely for the benefit of CLIENT.

2.3. Regulatory Matters.

(a) Unless otherwise specified in an individual Task Order, CLIENT will be responsible for all written and oral contact with any Agencies with respect to the Services and any Deliverable and the preparation and submission of all other reports or notices required by the Laws.

As between the parties, CLIENT shall have the sole right to prepare and file for the Health Registrations, including the CMC, with the applicable Agencies, and, for clarity, PROVIDER shall have no right to do so and shall not communicate with any Agencies in connection with any Health Registration. PROVIDER shall not initiate any communications with any Agency concerning any of the Services, a Project or a Deliverable without first getting written consent from CLIENT unless such communication is required by Law (in which case PROVIDER shall give as much prior written notice of such communication as possible) or requested to do so by CLIENT at CLIENT'S reasonable cost. If determined by CLIENT (in its sole discretion), CLIENT shall have the right to include a designation of PROVIDER and the Facility as a Manufacturer and Manufacturing site of Product in the applicable Health Registrations.

(b) PROVIDER shall promptly inform CLIENT of any request or effort by any Agency to contact, visit, or inspect PROVIDER, the Facility, the Records or other relevant information relating to or impacting any of the Projects or PROVIDER'S performance of Services, or take any other regulatory action. PROVIDER shall notify CLIENT within [***] if any Agency, including any regulatory authority, issues or gives to PROVIDER any notice of intent to inspect, notice of inspection, notice of inspection observations, warning letter, or other written communication concerning any of the Services.

(c) PROVIDER will provide to CLIENT or directly to the Agency, as requested, at CLIENT'S expense, which shall be described in an applicable Task Order, information in PROVIDER'S control necessary for CLIENT to apply for, obtain and maintain regulatory approvals, including any Health Registration. PROVIDER shall inform CLIENT prior to making commitments to any Agency relating to changes in Services planned to be performed at PROVIDER'S facility.

(d) CLIENT, in its discretion, may provide PROVIDER with CMC information applicable to aid PROVIDER in the development of the Master Batch Records used in the Manufacture of Product in accordance with this Agreement and applicable Law. For clarity, all CMC information shall be considered Confidential Information of CLIENT hereunder.

(e) Upon request, PROVIDER shall perform any applicable Services (including testing and, at CLIENT'S request, preparing documents to support CMC modules for filing or filing related support for the Health Registrations) in connection with the application, receipt, and maintenance of any Health Registrations for Product as set forth and described in the applicable Task Order or as otherwise requested in writing by CLIENT from time to time, at CLIENT'S reasonable cost (which may be set forth in a new Task Order), which activities shall be performed by PROVIDER in compliance with all applicable Laws. In all cases, PROVIDER shall be prepared for any and all inspections, including pre-approval inspections, by Agencies. As mutually agreed to and as described in a relevant Task Order, or as otherwise requested in writing by CLIENT from time to time (which may be set forth in a new Task Order), at CLIENT'S reasonable cost, PROVIDER shall provide CLIENT with such information and assistance as CLIENT may reasonably request for purposes of applying for and maintaining all relevant Health Registrations for Product including providing CLIENT with any applicable reports, authorizations, certificates, methodologies, specifications and other documentation in the possession or under the control of PROVIDER (or any of its Affiliates) relating to the pharmaceutical/technical development and/or Manufacture of Product or any component thereof.

(f) PROVIDER acknowledges that Agencies may, in conducting an inspection of CLIENT, request copies of reports of CLIENT audits of its suppliers, including PROVIDER. For clarity, in response to such a request, CLIENT shall have the right to provide to the Agency any

report of any compliance audit conducted hereunder (including as may be conducted in accordance with the Quality Agreement) and any other information in connection with the activities hereunder and shall notify PROVIDER of such request by the Agency.

(g) CLIENT shall be responsible for conducting any recall of Product, managing all returns of Product, and managing all customer, healthcare provider or patient technical and quality complaints related to Product, including complaints related to the ingredients or components of Product. In such cases above and at CLIENT'S request, PROVIDER shall co-operate with and give reasonable assistance to CLIENT, at CLIENT's reasonable expense (which shall be described in a Task Order or otherwise agreed by the parties in writing), in conducting any such recall, managing such return, or managing such complaints related to Product. For recalls that occur within the latent defect period described in Section 5.4, and to the extent the results of the applicable investigation determine that PROVIDER is at fault, the remedies in Section 8.3 shall apply. For recalls that occur after the latent defect period described in Section 5.4, and to the extent the results of the investigation determine that PROVIDER is at fault, PROVIDER shall, proportionally to PROVIDER'S fault, reimburse CLIENT for all the applicable investigation costs, but the remedies in Section 8.3 shall not apply.

2.4. Standard Operating Procedures.

(a) If a Law is amended or comes into existence which affects PROVIDER'S performance under this Agreement, and PROVIDER is made aware of such amendment or new Law (a "Law Modification"), then PROVIDER shall notify CLIENT in writing of such Law Modification. If either party believes a material change, modification or amendment to its own SOPs that impact the Services is necessary to comply with the Law Modification, the parties will follow the Change Order process described in Section 2.5 below. Only if and to the extent so required to comply with the applicable Law Modification, PROVIDER shall have no obligation to continue performing the Services (and CLIENT shall pay all invoices issued for any Services provided in accordance with this Agreement up to the Law Modification which require PROVIDER to pause the performance of the Services pursuant to this Agreement) while any Change Order is being discussed if such Change Order is required to comply with the Law Modification.

(b) Each party's SOPs shall be deemed to be the confidential information of that party and subject to the provisions of Article 7 hereof.

2.5. Changes to Task Orders. If any changes, modifications, or amendments to a Task Order (each a "Change") are required, the requesting party shall provide written notice to the other party in accordance with the procedures set forth below:

(a) A Change proposed by either party shall be initiated by written notice to the other party ("Change Order"). Each Change Order shall detail the specific changes to the applicable Task Order, including the changes to the specific Services to be performed, changes to either party's responsibilities or obligations, or any changes to the applicable timeline or Project Budget.

(b) Within [***] of PROVIDER'S receipt of a Change Order initiated by CLIENT or as part of any Change Order proposed by PROVIDER, PROVIDER shall furnish CLIENT with an estimate of the amount of time necessary to implement such Change and the effect, if any, of the Change(s) requested in the Change Order upon the applicable Budget (whether an increase or decrease). Following CLIENT'S review of PROVIDER'S estimate, the Change

Order shall be deemed to be approved and PROVIDER is authorized to proceed with the Change upon signature of authorized representatives of both PROVIDER and CLIENT.

(c) In addition to the items noted above, a Change Order initiated by PROVIDER and provided to CLIENT shall contain, in reasonable detail, the reason for the Change(s) and an estimate of the effect of the Change(s), if any, on the applicable Budget (whether an increase or decrease). Upon CLIENT'S written approval of PROVIDER'S estimate, the Change Order shall be deemed to be approved and PROVIDER may proceed with the Change. Nothing herein shall require the CLIENT to agree to any Change Order proposed by PROVIDER.

(d) Change Orders for a particular Project and/or Task Order(s) performed for a CLIENT Affiliate shall be signed by an authorized representative of the Affiliate for such Project and shall not require the signature of CLIENT or any other CLIENT Affiliate.

2.6. Initial Scope of the Agreement. As currently written, the Agreement shall be used solely for Process Development Services, Services related to the Manufacture of Product for use in human clinical trials, and other Services that are related to Agency pre-approval activities. This Agreement specifically excludes commercial supply of Product following Agency clearance or approval commercial supply of Product. In order for PROVIDER to Manufacture and supply such commercial Product, the parties need to enter into a separate written agreement for such commercial supply of Product ("Commercial Supply Terms"). If CLIENT so requests, the parties shall enter into good-faith, best efforts negotiations to come to mutually agreeable Commercial Supply Terms in a timely manner.

2.7. Communication with Agencies. As between the parties, CLIENT shall have the sole right to communicate with the appropriate Agencies relating to Product, and PROVIDER shall have no right to do so. PROVIDER shall provide CLIENT or its Affiliate, promptly, all information in PROVIDER'S (or its Affiliates' or subcontractors') possession or control concerning Product which is reasonably requested by CLIENT (or its Affiliates) and which is reasonably necessary to meet CLIENT'S (and its Affiliates') regulatory obligations. PROVIDER shall, to the extent such notice is not prohibited by applicable Law, notify CLIENT within [***] of any Agency request for samples of Product or Manufacturing Batch records or any other information related to Product and will not provide such material, records or information until such notification is made to CLIENT.

ARTICLE 3 - PROVIDER RESPONSIBILITIES

3.1. Personnel. PROVIDER shall be responsible for ensuring that a sufficient number of trained and qualified personnel are assigned to the Services, in order to perform the Services required therefore in accordance with this Agreement and otherwise meet the demands of the Services. PROVIDER may not subcontract, delegate or otherwise assign the performance of any of the Services (other than to an Affiliate) without the prior written consent of CLIENT, which consent shall not be unreasonably withheld, conditioned or delayed.

3.2. Reports. For each Project for which Services are performed, PROVIDER shall:

(a) provide CLIENT with status reports regarding the Services performed in accordance with the relevant Task Order;

(b) upon completion of the Services performed by PROVIDER, prepare and submit to CLIENT a draft final Report. The form of the draft final Report and the topics addressed therein shall comply with any reasonable directives of CLIENT. Within [***] or unless as otherwise described in the relevant Task Order, CLIENT shall use commercially reasonable efforts to either approve same or provide PROVIDER with its comments. PROVIDER shall submit to

CLIENT for its review and comment the revised final Report within [***] of receipt of CLIENT'S approval or comments on the draft.

(c) Any reports related to regulatory or quality shall also be addressed according to applicable requirements in the Quality Agreement.

3.3. Records. PROVIDER shall maintain complete and accurate production records, including Production Records, that would enable an independent auditor to verify the results of said Service(s) and as required to comply with applicable Law ("Production Notes"). The Production Notes shall be maintained by PROVIDER for [***] following the completion of the applicable Service or such longer period as required by any applicable Law. For storage beyond such period referenced above, PROVIDER shall charge CLIENT a storage fee at no more than PROVIDERS then prevailing storage fee rates.

(a) Without limitation of Section 3.4 or Section 3.3(b), PROVIDER agrees to permit CLIENT or its representatives to review the Production Notes at no charge to CLIENT, with prior written notification and during normal business hours. To the extent that the activities of PROVIDER hereunder include: (i) access by CLIENT to a website, database, server or other service which will cause PROVIDER to be in possession of any information belonging to CLIENT or which CLIENT is required to safeguard or maintain; or (ii) other activities which require or permit PROVIDER to electronically store, access or transmit information belonging to CLIENT or which CLIENT is required to safeguard or maintain, CLIENT shall have the right, but not the obligation, as only as part of the annual Quality audit, to conduct a data security audit of PROVIDER'S systems and premises to evaluate PROVIDER'S anti - virus, anti-hacker, encryption, firewall and other data security technology, and general computer controls, measures and practices. For clarity, any such inspection (or failure to inspect) shall not relieve PROVIDER of its obligation to comply with applicable Laws and the provisions of this Agreement and does not constitute a waiver of any right otherwise available to CLIENT.

(b) PROVIDER shall provide CLIENT on a periodic basis, and at least annually, or as otherwise requested by CLIENT from time to time, such information concerning Product, production Batches, yields and quality status as is specified in the Health Registrations or as otherwise may be reasonably requested by CLIENT from time to time.

(c) Prior to destruction of any Records, PROVIDER shall give notice to CLIENT at the last known contact information and address of CLIENT, and CLIENT shall have the right to take possession thereof within [***] of such notification.

(d) PROVIDER and CLIENT will each maintain records necessary to permit a Recall of any Products delivered to CLIENT or customers of CLIENT.

3.4. CLIENT'S Right to Audit and Visit.

(a) Visits: Upon no less than [***] advance notice or a shorter time as mutually agreed to by the parties, and for good cause, and at mutually agreeable times and dates during normal business hours, PROVIDER will permit CLIENT representatives or designees to visit PROVIDER facilities relevant to the Services, discuss the Project with appropriate officials of PROVIDER, and review records and data relevant to the Project, including the Production Notes (subject to the confidentiality obligations of this Agreement). PROVIDER shall retain the right to charge CLIENT for costs associated with such visit unless such visit is "for cause", which shall be described in a Task Order. Facility visits shall also be permitted during the data retention period described in Section 3.3 above.

(b) Quality Audits: As described in the Quality Agreement and no more than [***], upon no less than [***] advance notice, CLIENT, or an authorized agent of CLIENT, at any time upon reasonable advance notice to PROVIDER, at mutually agreeable dates and times during normal business hours, shall have the right to conduct a not-for-cause audit of PROVIDER'S facilities at which any of the Services are performed, including the Facility, and of any and all records and data relating to any Project, including Production Notes and Manufacturing Records, and discuss the Project with appropriate officials of PROVIDER, for the purposes of:

(i) verifying PROVIDER'S compliance with this Agreement (including compliance with all Laws); and

(ii) evaluating the analyses and testing and the resulting information obtained thereby in the performance of the Services.

(c) PROVIDER shall reasonably cooperate with CLIENT in any visit or audit conducted hereunder and take reasonable steps to resolve any unsatisfactory audit findings. In the event CLIENT identifies any deficiency with respect to PROVIDER's operations or activities during any such visit, inspection, audit, or review, CLIENT shall have the right to notify PROVIDER of such deficiency, and, in such case, PROVIDER shall, within [***] from the date of receipt of such notice, deliver to CLIENT a corrective action plan, addressing each such deficiency. Upon acceptance of the corrective action plan by CLIENT (which acceptance shall not be unreasonably withheld), PROVIDER shall fully implement such corrective action plan to the reasonable satisfaction of CLIENT; provided, however, that CLIENT may (but shall not be obligated to), in its sole discretion, accept Product from PROVIDER prior to PROVIDER'S completion of the corrective action. CLIENT shall have the right to review all relevant documentation in connection therewith. All audits conducted pursuant to this Agreement shall be subject to the confidentiality obligations set forth in this Agreement and to CLIENT'S compliance with PROVIDER'S safety, security and other policies applicable to the Facilities where such audits are performed. As part of the visit or audit, CLIENT shall not copy, attempt to copy, photograph, attempt to photograph, reproduce, replicate, attempt to reproduce or reverse engineer any PROVIDER Technology.

(d) "For cause" audits will be scheduled on an expedited basis as soon as commercially reasonable and may be conducted as needed.

(e) As mutually agreed to by the parties (such agreement by PROVIDER not to be unreasonably withheld, conditioned or delayed), and as described in a task order (as applicable), during the term of this Agreement during which Manufacturing activities are taking place, CLIENT shall be allowed to have representatives on site at the Facility and access to all associated records, for the purpose of observing, reporting on, and consulting as to any Manufacturing activities hereunder.

3.5. Agency Audits and Inspections.

(a) PROVIDER shall permit Agencies to have access to and inspect the Facility or Facilities at which any of the Services are performed and to any and all data and Records maintained by PROVIDER for the Services. PROVIDER will notify CLIENT promptly (in any event within [***]) or as described in the Quality Agreement upon its knowledge of an Agency audit or inspection. PROVIDER shall cooperate with the Agency and allow them access to the relevant information. PROVIDER shall ensure that no more than three representative(s) of CLIENT (or its Affiliates or designees), or as mutually agreed to by both parties, may be present on-site at any such visit or inspection, if requested by CLIENT, provided that

CLIENT (or its Affiliates or designees) does not interact with said Agency during the visit or inspection unless authorized to do so, in writing, by PROVIDER or required to comply with applicable Law.

(b) PROVIDER shall promptly provide CLIENT with any or all copies of information provided to or received by PROVIDER in the course of an Agency audit or inspection that directly relates to CLIENT'S Services or Product as described in the Quality Agreement or as otherwise required to comply with Law, which may include FDA Form 483s, Establishment Inspection Reports, or warning letters. PROVIDER shall consult with CLIENT in an effort to arrive at a mutually acceptable response to the extent related to CLIENT'S Product. PROVIDER shall promptly inform CLIENT of any request or effort by any Agency to contact, visit, or inspect PROVIDER, the Project Records or other relevant information relating to any of the Projects or PROVIDER's performance of Services or to take any other regulatory action. PROVIDER shall retain the right to charge CLIENT for regulatory support or fees for follow- on Services, which shall be described in a Task Order, resulting from such Agency audits or inspections, except to the extent such Agency audit or inspection is due to PROVIDER'S breach of this Agreement or the gross negligence, intentional misconduct or violation of Law of the PROVIDER or any person or entity for which PROVIDER is responsible (in which case PROVIDER shall bear such costs).

ARTICLE 4 - GENERAL PRODUCTION SERVICE REQUIREMENTS

PROVIDER, if requested by CLIENT in connection with an individual Task Order, shall perform some or all of the related services described in this Article 4, as required in the applicable Task Order.

4.1. Storage and Shipping of CLIENT Materials, CLIENT Deliverables, Data Exchange. If agreed in a Task Order, PROVIDER shall:

(a) maintain a validated cGMP-compliant storage system (including continuous monitoring) by which CLIENT Materials are stored and analyzed at specified temperatures within the stability period. Following disposition of the Batch, PROVIDER, as applicable, shall store CLIENT Materials for analysis and/or archival reference in secured freezers with appropriate temperature monitoring and recording for a period of [***]. Prior to the end of the [***] period, CLIENT shall instruct PROVIDER to ship or destroy any remaining CLIENT Material, at CLIENT'S expense. In the absence of instructions from CLIENT, PROVIDER shall automatically charge CLIENT PROVIDER'S reasonable applicable storage fees for the storage of remaining CLIENT Materials. Upon mutual agreement by the parties via an applicable Task Order, PROVIDER will store CLIENT Materials beyond the [***] period, at CLIENT'S expense. NOTWITHSTANDING ANY PROVISIONS DESCRIBED IN SECTION 9, PROVIDER'S AGGREGATE LIABILITY FOR ANY AND ALL CLAIMS, BUT NOT INCLUDING CLAIMS RELATED TO PROVIDER'S VIOLATION OF LAW, GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, ARISING OUT OF OR IN CONNECTION WITH THE STORAGE OF CLIENT MATERIALS OR CLIENT DELIVERABLES, INCLUDING BUT NOT LIMITED TO DRUG SUBSTANCE OR PRODUCT, SHALL NOT EXCEED $[***] (USD). Prior to destruction of any stored CLIENT Materials or Deliverables, PROVIDER will notify CLIENT in writing and CLIENT shall have the right to direct whether such CLIENT Materials or Deliverables will be sent to CLIENT or destroyed in compliance with applicable Laws at CLIENT'S reasonable expense. PROVIDER shall document in writing the monitoring of storage of any CLIENT Materials and Deliverables, and at CLIENT'S request, PROVIDER shall provide CLIENT with a copy of such written monitoring documentation;

(b) be responsible for arranging for express shipping services by a Third Party who provides a system by which CLIENT Materials can be tracked and temperature monitored during

shipment for all CLIENT Materials shipped between PROVIDER and CLIENT and/or any Third-Party laboratory designated by CLIENT. It is understood that CLIENT shall bear the risk of loss of, or damage to, any CLIENT Materials during shipment;

(c) obtain CLIENT'S written consent for any special shipping procedures required on Sundays and holidays which entail additional expense;

(d) make any arrangements requested by CLIENT in order to accommodate and coordinate data exchange (including electronic data transfer) between PROVIDER and CLIENT and any other Third-Party laboratory designated by CLIENT; and

(e) obtain data clarification for all Services and testing procedures described in the relevant Task Order and/or other analytical methodology approved or provided by CLIENT.

4.2. Technical Transfer; Process Development.

(a) General. The parties shall engage in the Technical Transfer as described in the applicable Task Order(s). In performing the Technical Transfer, the parties, respectively, shall use commercially reasonable effort to perform such tasks as are set forth in and as are in accordance with the estimated timelines described in the applicable Task Order(s). Each party shall reasonably cooperate with the other party to provide appropriate information and assistance to the other party in connection with the Technical Transfer.

(b) Contacts; Meetings. Each party will appoint a "program manager" having primary responsibility for day-to-day interactions with the other party for the Technical Transfer. Except for notices or communications required or permitted under this Agreement, which shall be subject to Section 11.9 below, all day-to-day, routine communications between PROVIDER and CLIENT regarding the execution of the Technical Transfer will be addressed via the party's relevant program manager or within the joint project teams. The parties will hold regular project team meetings via teleconference or in person, on a periodic basis as agreed by the program managers.

(c) Process Development.

(i) As described in an applicable Task Order(s), CLIENT may engage PROVIDER to provide Process Development Services.

(ii) Following completion of any Process Development Services, PROVIDER shall use commercially reasonable efforts to provide CLIENT with any applicable document Deliverables as described in the relevant Task Order(s).

(iii) Upon request, PROVIDER shall perform one or more process development and/or engineering runs and Manufacture non-cGMP process development and/or engineering Batches of Product in accordance with the relevant Task Order(s). PROVIDER shall perform any applicable analytical testing of the Batch as agreed by the parties in each Task Order and will report the results to CLIENT. CLIENT shall have the right to make whatever further use of such process development and/or engineering Batches as it shall determine, provided that such use does not violate any applicable Laws.

4.3. Location of Manufacturing Activities. Notwithstanding anything to the contrary contained herein, all Manufacturing activities shall occur at the Facility and PROVIDER may not change to a different facility (for all or any portion of the Manufacture of Product hereunder) unless consented to by

CLIENT in writing (in its sole discretion); provided, that in all cases no change of Facility shall relieve PROVIDER of any of its obligations under this Agreement; provided, further, that all changes shall also be in accordance with Section 2.5, to the extent applicable. PROVIDER shall provide to CLIENT supporting data in order to permit CLIENT to amend its (and its Affiliate's and designee's, as applicable) regulatory filings to reflect any such change and shall otherwise cooperate in good faith with CLIENT to comply with all regulatory obligations arising out of such changes. Any applicable charges associated with said Facility change will be described and mutually agreed to in a Task Order.

4.4. CLIENT Materials.

(a) The Task Order for a given Product shall set forth any CLIENT Materials, including Drug Substance and/or Drug Product and intermediates (if any), to be supplied by or on behalf of, CLIENT to PROVIDER for use in the Process Development Services or Manufacture of such Product hereunder. CLIENT Materials shall at all times remain the property of CLIENT (and PROVIDER shall ensure that no pledges, liens, restrictions, claims, charges, security interests or other encumbrance are placed on such CLIENT Materials, other than by CLIENT or its Affiliate). Without limiting the foregoing, CLIENT shall have the option (in its discretion) from time to time, upon prior written notice to PROVIDER, to provide certain other CLIENT Materials for use in the Process Development Services or Manufacture of Product hereunder. Any additional costs associated with the supply of CLIENT Materials to PROVIDER shall be borne by the CLIENT and any PROVIDER fees previously payable for such CLIENT Materials shall not be charged, less any fees for material handling or applicable testing.

(b) PROVIDER shall use CLIENT Materials solely and exclusively for Process Development Services or to Manufacture Products under this Agreement and the applicable Task Order, as applicable, and for no other purpose. When reasonably practical, PROVIDER shall withdraw CLIENT Materials from storage respecting the procedure of first expiry/first out or as mutually agreed by the parties.

(c) All CLIENT Materials shall be handled, stored and maintained by PROVIDER in accordance with PROVIDER SOPs and applicable Laws (including cGMPs). CLIENT shall provide to PROVIDER material safety data sheets relating to CLIENT Materials, and other information known to CLIENT relating to handling, environmental, health and safety ("EHS") precautions with respect to CLIENT Materials. It is the sole responsibility of the PROVIDER to communicate such information to its employees, agents, subcontractors, and representatives engaged in performing the Services and furthermore PROVIDER shall ensure that all safety and other SOPs are followed by PROVIDER and its employees, agents, subcontractors, and representatives.

(d) Notwithstanding anything to the contrary contained herein, in the event that CLIENT fails to supply quantities of CLIENT Materials it is require to provide hereunder sufficient for Process Development Services or to Manufacture Product, then CLIENT shall not be deemed to be in breach of this Agreement or applicable Task Order, and the CLIENT shall only be subject to any applicable cancellation, termination, or delay fees, if any, as described in Section 10.3 or Section 10.6 for the applicable Services.

(e) PROVIDER shall immediately return to CLIENT, or dispose of, CLIENT Materials upon request by CLIENT (as and to the extent requested by CLIENT). Any such disposal (if disposal is requested by CLIENT) shall be done in compliance with applicable Laws.

4.5. Acceptance and Use of Drug Substance and/or Drug Product. Unless mutually agreed to by the parties, to the extent that Drug Substance and/or Drug Product is included as part of CLIENT Materials to be supplied by the CLIENT hereunder with respect to a given Product, then each delivery of Drug Substance and/or Drug Product to PROVIDER will be accompanied by a certificate of [***]and PROVIDER shall not incorporate any Drug Substance and/or Drug Product into the Manufacture of Product that is not accompanied by a certificate of [***]. Before incorporating any such Drug Substance and/or Drug Product into the Manufacture of Product, PROVIDER shall conduct reasonable quality control inspection or testing, which tests shall, in any event, include those tests identified in: (a) applicable Technical Specifications; (b) the Quality Agreement as the responsibility of PROVIDER; and/or (c) written instructions provided by CLIENT from time-to-time. PROVIDER shall promptly (and described in the Quality Agreement) notify CLIENT of any Drug Substance and/or Drug Product that does not meet the Technical Specifications and PROVIDER shall not use any such Drug Substance and/or Drug Product in its Manufacturing hereunder.

4.6. Handling, Storage and Use of CLIENT Materials. PROVIDER shall handle, use and store CLIENT Supplied Materials under suitable conditions at the Facility and in accordance with the applicable handling and storage requirements, if any, set forth on the applicable Task Order or as otherwise provided by CLIENT in writing from time to time, as well as all applicable Laws and the applicable Specifications and Health Registrations. PROVIDER shall use CLIENT Supplied Materials only for the Manufacture of Product hereunder and for no other purpose. In accordance with Section 3.4 and upon prior written request by CLIENT, at reasonable times and upon reasonable notice CLIENT shall have the right to visit the Facility where CLIENT Materials are being stored to inspect and/or conduct and inventory of CLIENT Materials and the conditions of handing, use and storage thereof, without interruption to the business operations of PROVIDER. Upon the prior written request of CLIENT, PROVIDER shall immediately stop using any given CLIENT Supplied Materials (as directed in such notice) and PROVIDER shall, at the direction of CLIENT, either return to CLIENT or destroy such CLIENT Supplied Materials pursuant to CLIENT'S reasonable instructions.

4.7. PROVIDER Supplied Materials.

(a) PROVIDER Supplied Materials Generally. PROVIDER shall be responsible for procuring the supply of all materials and components, necessary for the Process Development Services and Manufacture of Product in accordance with this Agreement, other than any CLIENT Materials specified in the applicable Task Order to be provided by the CLIENT ("PROVIDER Supplied Materials"). All PROVIDER Supplied Materials shall, in all cases, be in compliance with all applicable Laws and the applicable Technical Specifications, and Health Registrations.

(b) PROVIDER Supplied Materials Documentation. PROVIDER shall have adequate procedures for evaluating the quality of the suppliers of PROVIDER Supplied Materials and shall have documents indicating that evaluations were conducted in accordance with such procedures.

4.8. Quality Agreement. No later than [***] after the effective date of the first Task Order (or such other time as agreed to by the parties but in all cases prior to the start of activities in support of GMP Manufacturing), the parties shall enter into a Quality Agreement.

ARTICLE 5 - GENERAL MANUFACTURING REQUIREMENTS

5.1. General Provisions. Except as expressly permitted in this Agreement, neither party shall make changes to the Production Records or the Specifications without the prior written approval of the other party, which approval will not be unreasonably withheld. PROVIDER shall make no changes in the SOPs, production equipment, production procedures, or testing methods existing as of the

date of this Agreement which materially affect the Services without providing reasonable notice to CLIENT in advance of the change and obtaining CLIENT'S prior written consent, which will not be unreasonably withheld. PROVIDER shall maintain all Records as are necessary and appropriate to demonstrate compliance with the Laws, including cGMP. CLIENT shall be entitled to request PROVIDER to change the Specifications and the SOPs, and PROVIDER shall use commercially reasonable efforts to accommodate such change; provided that CLIENT will reimburse PROVIDER for actual, out-of-pocket costs incurred in making any such change; provided further that the parties shall engage in good faith negotiations to adjust the Budget to reflect the increase or decrease of ongoing costs hereunder resulting from any such change; provided further that if the parties cannot reach agreement to adjust the Budget pursuant to this Section 5.1 despite such good faith negotiations, then PROVIDER shall not be required to change the Specifications or SOPs as requested by CLIENT until the parties reach such agreement.

(a) CLIENT reserves the right upon reasonable advance written notice to PROVIDER to amend and/or supplement: (i) the Drug Substance and/or Drug Product; (ii) the materials used to Manufacture the Deliverable(s); (iii) the source of the materials used to Manufacture the Deliverable(s) and/or Drug Substance and/or Drug Product; (iv) the specifications for materials used to Manufacture the Deliverable(s); (v) the equipment used in Manufacturing Product; (vi) the test methods used in connection with the Manufacturing of Product, Drug Substance and/or Drug Product or materials used to Manufacture the Deliverable(s); (vii) the process for Manufacturing Product, Drug Substance and/or Drug Product or materials used to Manufacture the Deliverable(s); and/or (viii) any test methods used in the Manufacturing, release or testing the stability of Product and/or Drug Substance and/or Drug Product. Upon receipt of such notice, PROVIDER shall promptly acknowledge in writing and implement such modifications within an agreed upon timeline, as set forth in such notice. PROVIDER shall ensure that any change in any of the foregoing shall, in each case, comply with cGMPs and all other applicable Laws.

(b) The costs of implementing any of the changes referred to in this Section 5.1 shall be borne solely by CLIENT.

5.2. Testing Deliverable. As specified in the Task Order, with respect to each shipment of Deliverable to be shipped to CLIENT, PROVIDER shall test such Deliverable as specified in the Task Order or Quality Agreement to ensure compliance with the Technical Specifications, the other requirements of this Agreement and applicable Laws. With respect to each shipment of Product, PROVIDER shall provide CLIENT with a Certificate of [***] from PROVIDER'S quality assurance department that: (a) includes the results of quality control testing, including applicable analytical testing, in accordance with the Technical Specifications; and (b) indicates that Product contained in such shipment (i) meets the applicable Technical Specifications, and (ii) has been Manufactured in compliance with this Agreement, the relevant Task Order, the Quality Agreement, the Technical Specifications, , and applicable Laws (including cGMPs).

5.3. Acceptance. Subject to Section 5.4 below, CLIENT shall have a period of [***] following disposition of the Batch to inspect such delivered Deliverable and the accompanying Certificate of [***] and reject the corresponding shipment of Deliverable for nonconformity with the Technical Specifications, the other requirements of this Agreement or applicable Laws. If CLIENT rejects such Deliverable, it shall promptly so notify PROVIDER and provide sufficient detail of the nonconformity, and the provisions of Section 8.3 below shall apply.

5.4. Latent Defects. If within [***] after accepting a shipment of Deliverable(s), CLIENT subsequently discovers latent defects not reasonably discoverable during the acceptance period set forth in Section 5.3 above, CLIENT may revoke its acceptance of such shipment of Deliverable by giving

written notice and disclosing the nature of any defects to PROVIDER immediately after discovering such defects.

5.5. Deviation Report. If during the Manufacture, including the processing, storage, distribution, testing, transport, disposal or other handling, of a Deliverable by PROVIDER there arises an unexpected result that has an unknown or potential serious impact on product safety, identity, strength, quality, purity, efficacy or manufacturing/testing process, then PROVIDER shall prepare promptly, as defined in the Quality Agreement and following the discovery of such deviation, a written report detailing such deviation (a "Deviation Report") and promptly send to CLIENT such Deviation Report prior to any delivery of the Deliverable which is the subject of such report. If CLIENT rejects a Deliverable based on a Deviation Report, it shall promptly notify PROVIDER, such Deliverable shall be considered a Nonconforming Product and the provisions of Section 8.3 shall apply. PROVIDER agrees not to reprocess or rework any Batch of Product, or any intermediate in the Manufacture of Product, without the prior written approval of CLIENT (in its sole discretion) in writing.

5.6. Independent Laboratory. Notwithstanding anything in this Agreement to the contrary, if PROVIDER does not agree that any Deliverable failed to meet the Technical Specifications or that any Deliverable is otherwise a Nonconforming Product, and the parties cannot reach agreement with respect to such Deliverable, PROVIDER will submit the dispute to an independent laboratory mutually agreed to by the parties for determination. The findings of such laboratory shall be binding the parties, absent fraud or manifest error on the part of the independent laboratory, and the cost of such determination shall be paid by the party in error. The laboratory shall make its determination solely based upon whether the Deliverable meets the Technical Specifications, the Quality Agreement requirements, and the Laws in effect at the time of Manufacture or otherwise fails to meet the warranty in Section 8.3. Upon resolution of any such dispute in favor of PROVIDER, CLIENT shall pay the full cost of the independent laboratory testing in addition to paying the full invoice amount properly due and/or remaining for such Deliverable within [***] after such resolution. Upon resolution of any such dispute in favor of CLIENT, PROVIDER will as soon as commercially reasonable, replace such Non-conforming Product with an equivalent amount of Conforming Product and pay the full cost of the independent laboratory testing. In addition to the above, PROVIDER will, at its sole cost and expense, destroy all Nonconforming Product in its possession and promptly provide a certificate of destruction to CLIENT. For clarity, the foregoing provisions of this Section 5.6 shall not limit any rights or remedies of CLIENT with respect to any defective or Nonconforming Product or other Deliverable supplied hereunder.

5.7. Acceptance of Documentation Deliverables. Following PROVIDER'S delivery of each Deliverable that is a documentation, including report, records or other documents or information (each, a "Documentation Deliverable"), CLIENT (with the assistance of PROVIDER, if so requested) will have a [***] period to review and evaluate each Documentation Deliverable to confirm that such Documentation Deliverable satisfies the applicable acceptance criteria, specifications and requirements for such Documentation Deliverable, as specified in the applicable Task Order (collectively, the "Acceptance Criteria"). If the Documentation Deliverable fails to satisfy the applicable Acceptance Criteria or requires any correction, then CLIENT will promptly notify PROVIDER in writing and identify the specific defects in or correction needed for the Documentation Deliverable. Upon receipt of such a notice, PROVIDER will use commercially reasonable efforts promptly to revise the Documentation Deliverable and re-submit the Documentation Deliverable to CLIENT in accordance with the terms of this Section 5.7.

5.8. Notification of Defects by PROVIDER. If PROVIDER discovers that any Batch of Product previously delivered to CLIENT under this Agreement is Nonconforming Product or there are other safety or efficacy concerns with respect to the Product, then PROVIDER shall immediately (and in all cases

within [***]) notify CLIENT of such failure or concern, and PROVIDER shall consult with CLIENT in connection therewith.

5.9. Products Returned to PROVIDER. In the event that PROVIDER receives any returned Product from a Third Party, then PROVIDER shall promptly notify CLIENT in writing of such returned Products, and, at CLIENT'S discretion, shall destroy or return such returned products to CLIENT (or its designee). In all cases, PROVIDER shall promptly provide to CLIENT all documentation received with such returned products.

ARTICLE 6 - COMPENSATION AND PAYMENT

6.1. Budget. PROVIDER shall prepare and submit to CLIENT for its approval a budget for each Project including PROVIDER'S fees, non-refundable deposits (if any), deposits of any other kind, and any pass-through expenses which shall be agreed upon by the parties and form part of the relevant Task Order ("Budget"). A Budget may be amended from time to time in accordance with the Change Order process described in Section 2.5. Notwithstanding the foregoing, all deposits received by PROVIDER from CLIENT pursuant to this Agreement are non-refundable unless expressly stated in the Budget, yet are creditable towards any Delay or Cancellation Fees described in Section 10.

6.2. Compensation. As full and complete payment to PROVIDER for all Services provided by PROVIDER under this Agreement for each particular Project and for the assignment of any intellectual property rights as contemplated in Section 7.5, and subject to the provisions of Section 6.3 below, CLIENT shall compensate PROVIDER in accordance with the Budget for such Project as set forth in the relevant Task Order. CLIENT'S payments to PROVIDER under this Agreement are compensation for PROVIDER'S Services that have been provided to the CLIENT. CLIENT and PROVIDER hereby acknowledge and agree that any compensation payable to PROVIDER: (i) constitutes fair market value for the Services; (ii) is not being given in exchange for an explicit or implicit agreement by PROVIDER to provide favorable status to CLIENT or any of its products or to influence results; and (iii) has not been determined in a manner that takes into account the volume or value of any referrals generated by PROVIDER.

6.3. Invoicing and Payments. PROVIDER shall invoice CLIENT for expenses incurred, including non- refundable deposits (if any) or any other deposits of any kind, and Services performed for each Project in accordance with a payment schedule to be agreed by the parties and made a part of the relevant Task Order. All payments of undisputed amounts provided for under the terms of this Agreement shall be made within [***] of CLIENT'S receipt of each applicable invoice and by wire transfer payable to PROVIDER or its Affiliate, whichever is applicable to a Project or Task Order, as indicated on the invoice. If PROVIDER or its Affiliate does not receive payment of undisputed amounts by the due date, an interest charge may be added at the rate of [***] ([***]) or the maximum legal rate, whichever is less, to unpaid invoices from the due date thereof. Each invoice shall include (a) the name of PROVIDER, (b) a "Remit to" address, (c) CLIENT'S purchase order number (if any), (d) an invoice number, (e) an invoice date, (f) a description of the relevant goods, (g) total invoice amount (with separate line items for each charge), and (h) such other information as CLIENT may request.

6.4. Disputed Invoices. If any portion of an invoice is disputed, then CLIENT shall use commercially reasonable efforts to dispute such invoice in writing within [***] of receipt of such invoice and pay the undisputed amounts, and the parties shall use good faith efforts to reconcile the disputed amounts as soon as practicable. PROVIDER reserves the right to discontinue work wherein payments remain unpaid and the dispute remains unresolved for a period exceeding [***].

6.5. Taxes. CLIENT shall only be responsible for paying for value-added taxes, sales taxes and/or customs/duties imposed by the relevant taxing authority on payments made to the PROVIDER pursuant to this Agreement. All other taxes, such as income taxes, foreign withholding taxes, taxes related to PROVIDER'S revenues, gross receipts, personnel or real or personal property or other assets, etc., imposed on payments made to the PROVIDER pursuant to this Agreement shall be the sole responsibility of PROVIDER. If applicable Laws require that certain taxes be deducted and withheld from payments paid by CLIENT under this Agreement, CLIENT may: (a) deduct those taxes and interest and penalties assessed thereon from the payment or from any other payment owed by CLIENT hereunder; (b) pay those taxes to the proper governmental authority; (c) send evidence of the obligation together with proof of tax payment to PROVIDER following such payment; and (d) remit to PROVIDER the net amount, after deductions or withholding made under this Section 6.5.

ARTICLE 7 - CONFIDENTIALITY, PROPRIETARY RIGHTS, AND APPLICATION OF TECHNOLOGY

7.1. Confidentiality.

(a) As used in this Agreement, "CLIENT Confidential Information" means all information of CLIENT, its Affiliates and/or Business Partners, including information of Third Parties entrusted to any of the foregoing, which PROVIDER has received or will receive from or on behalf of CLIENT, its Affiliates and/or Business Partners or to which PROVIDER has access, during the term hereof, including all information received by PROVIDER from CLIENT under the terms of this Agreement (including pursuant to any confidentiality agreement entered into between CLIENT and PROVIDER prior to the date hereof), Project Records, and Project Reports, and any other proprietary information of CLIENT, including all CLIENT Technology. CLIENT Confidential Information also includes all Production Notes, Records, including Manufacturing Records, Products and other Deliverables. "PROVIDER Confidential Information" means PROVIDER Standard Operating Procedures and any and all information and/or other pre-existing proprietary or confidential information provided by PROVIDER to CLIENT under the terms of this Agreement including any information which a reasonable person would consider confidential or proprietary (including plans, designs, SOPs, specifications, technical analyses, data, drawings, pricing, raw material supply, and the like, whether tangible or intangible, written or oral).

(b) Each of PROVIDER and CLIENT agree that it shall keep confidential the Confidential Information of the other party and, other than as expressly permitted by this Agreement, shall not disclose the Confidential Information of the other party to any Third Party and shall not use the Confidential Information of the other party for any purpose other than to perform its obligations under this Agreement, except however, either party may disclose the terms of this Agreement to a bona fide Third Party suitor in connection with the sale of a party's business so long as the Third Party suitor is under confidentiality and non-use restrictions at least as strict as the ones herein. Also, CLIENT, as the recipient party, and its Affiliates and/or Business Partners shall have the right to use PROVIDER Confidential Information as necessary or useful to utilize the Services and otherwise exercise CLIENT'S rights under this Agreement. Further, each of PROVIDER and CLIENT shall limit disclosure of the Confidential Information of the other party to its Affiliates and those of its and their officers, directors, employees, consultants, advisors and agents (and in the case of disclosure by CLIENT to its Business Partners as well) ("Representatives") who have a "need to know" said Confidential Information for the purposes of this Agreement and who are subject to binding confidentiality obligations restricting their use and disclosure of such Confidential Information consistent with the provisions of this Agreement. Each party shall be responsible and liable for any disclosure or use by its Representatives of the other

party's Confidential Information in a manner not consistent with the restrictions set forth herein.

7.2. Exceptions. The foregoing confidentiality obligations shall not apply to Confidential Information to the extent the recipient party can establish by competent documentary proof that such Confidential Information:

(a) Was already properly known to the recipient party at the time of disclosure;

(b) Was generally available to the public or otherwise part of the public domain at the time of disclosure to the recipient party;

(c) Became generally available to the public or otherwise part of the public domain after its disclosure or development, as the case may be, and other than through an act or omission of the recipient party or any of its Representatives;

(d) Was properly disclosed to the recipient party by a third party who had no obligation to keep such information confidential to others; or

(e) Was developed independently by, or on behalf of, recipient party without use of, reference to, or reliance on the other party's Confidential Information.

Where the recipient party (or any of its Representatives) is required to disclose the other party's Confidential Information pursuant to applicable Laws, including any court or administrative proceedings or the like, the recipient party shall immediately notify the other party in writing of such requirement so that the other party has a meaningful opportunity to seek an appropriate protective order to prevent to such disclosure, and if so requested the recipient party shall cooperate in such efforts. If, after providing such notice and assistance as required herein, the recipient party (or any of its Representatives) remains legally required to disclose any Confidential Information, the recipient party (and its Representatives) shall disclose no more than that portion of the Confidential Information which, on the advice of the recipient party's legal counsel, the recipient party (or its Representatives) is legally required to disclose and, upon the other party's request, shall use commercially reasonable efforts to obtain assurances from the applicable court or agency that such Confidential Information will be afforded confidential treatment.

7.3. Publications. PROVIDER shall not publish any articles or papers nor make any presentations, nor assist any other person in publishing any articles or papers or in making any presentations, relating or referring to:

(a) Any of the Projects or any results, data or insights therefrom;

(b) Any of the Services performed by PROVIDER hereunder; or

(c) Any data, information or materials obtained or generated in the performance of PROVIDER'S obligations hereunder,

in whole or in part, without the prior written consent of CLIENT, which consent may be granted or withheld in CLIENT'S sole discretion.

7.4. Proprietary Rights.

(a) Except as expressly set forth in this Agreement, each party owns, and shall continue to own its pre-existing intellectual property, without conferring any interests therein on the other party.

(b) In performing the Project and/or in applying PROVIDER Technology to performance of the Services, including the Manufacture of the Deliverable, PROVIDER may develop ideas, know-how, inventions, techniques, improvements and other technology, whether or not patentable or copyrightable, and associated intellectual property that generally relate to the processes used by PROVIDER in its performance of the Project and/or in the conduct of PROVIDER'S business that are not CLIENT Inventions (collectively "PROVIDER Inventions"). All PROVIDER Inventions are and will remain the sole and exclusive property of PROVIDER and constitute Confidential Information of PROVIDER.

(c) Notwithstanding the foregoing, PROVIDER agrees that all intellectual property of any kind, including any and all improvements, (i) which encompasses, incorporates, or utilizes CLIENT Technology, including Product, CLIENT Material, or CLIENT Confidential Information or (ii) that is a Deliverable (collectively, all the foregoing, "CLIENT Invention(s)"), are and will remain the sole and exclusive property of CLIENT and constitute Confidential Information of CLIENT. Without limiting the foregoing, CLIENT Inventions shall include all required (for the performance of the Services) scientific, technical and other information, data, know-how, trade secrets, inventions (whether or not patentable), processes, compositions of matter, materials, methods, techniques, documentation, hardware, software and technology, and any other intellectual property rights, whether or not protected or protectable under patent, trademark, copyright or similar law, developed in connection with this Agreement that relates to, encompasses, incorporates, or utilizes the Drug Substance, Drug Product, or Product or relates in any way to CLIENT Confidential Information or CLIENT Technology.

(d) PROVIDER shall ensure that all of PROVIDER'S employees, agents and authorized subcontractors and any other person or entity for which PROVIDER is responsible are employed or engaged on terms consistent with this Section 7.4.

(e) In furtherance of the foregoing, PROVIDER shall, upon request by CLIENT, promptly undertake and perform (and/or cause its Affiliates and its and their respective Representatives to promptly undertake and perform, as applicable) such further actions as are reasonably necessary for CLIENT, as between the parties, to perfect its right and title in any CLIENT Inventions (and all intellectual property rights associated therewith), including by causing the execution of any assignments or other legal documentation, and/or providing CLIENT or its patent counsel with reasonable access to any Representatives who may be inventors of such CLIENT Inventions (and any intellectual property rights associated therewith). CLIENT agrees to reimburse any and all reasonable, out-of-pocket expenses incurred by PROVIDER in performing its obligations under this paragraph; provided, however, any fees and expenses of outside counsel or consultants and any travel expenses shall require prior written approval by CLIENT prior to being so reimbursable.

7.5. Application of Technology.

(a) To the extent that any CLIENT Technology is necessary or useful in order to facilitate PROVIDER to perform the Services, CLIENT hereby grants to PROVIDER a limited, non-exclusive license in and to any such CLIENT Technology for the sole purpose of performing

the Services. Except to the extent expressly set forth in this Agreement, this Agreement confers no license or intellectual property rights to or from either party.

(b) PROVIDER hereby grants to CLIENT a non-exclusive, royalty-free, fully paid-up, perpetual, non-terminable, worldwide license, with the right to grant sublicenses (single tier, unless further sublicensing is consented to by PROVIDER, such consent not to be unreasonably withheld, conditioned or delayed), and otherwise transfer such license to practice (including the right to make derivative works and copies of) any and all PROVIDER intellectual property, including PROVIDER Inventions, utilized in connection with this Agreement to make, have made, use, offer for sale, sell, and import limited to only (i) Products (including any Drug Substance or Drug Product) and any other products that incorporate or utilize any Products, and/or (ii) otherwise utilize all Deliverables specific to only the development and manufacture of Product(s) and/or any other products that incorporate or utilize any Products (including development and manufacture by the CLIENT, its Affiliates or Third Parties).

7.6. Equitable Relief. Each party hereby acknowledges and agrees that any actual or threatened breach of this Article 7 would cause irreparable harm to such other party for which remedies at law would not be adequate. Therefore, in the event of any such breach such other party shall be entitled to equitable relief, without having to post bond or other security or prove monetary damages, including an injunction, in addition to any and all other remedies available at law or in equity.

7.7. Privacy and Protected Health Information. If applicable to the performance of the Services, or if CLIENT incidentally or inadvertently provides PROVIDER with certain CLIENT Confidential Information which may qualify as Protected Health Information or PHI (defined below), CLIENT shall immediately inform PROVIDER or PROVIDER shall immediately inform CLIENT, whichever the case may be. PROVIDER agrees that it does not have a need to access or view any PHI to provide the Services, and it will not attempt to obtain access to any such PHI. With respect to any PHI that it may incidentally or inadvertently encounter, view or access, PROVIDER agrees to (a) comply with all applicable Law, including the Health Insurance Portability and Accountability Act of 1996, the Health Information Technology for Economic Clinical Health Act of 2009, and the EU Data Protection Law, as may be applicable, (b) keep the PHI confidential and not permit any Third Party access to such PHI, (c) implement and have in place appropriate measures to prevent misuse or unauthorized release of such PHI, (d) provide reasonable assistance to CLIENT as reasonably required by CLIENT, for CLIENT to address any PROVIDER unauthorized use or processing of PHI, and (e) process PHI only in accordance with CLIENT'S instructions and as mutually agreed between the parties. On the completion, expiration or termination of this Agreement, PROVIDER will, at CLIENT'S cost and expense, return any PHI to CLIENT save where such retention of PHI is required by PROVIDER to comply with its obligations under applicable Law or the Agreement or is incorporated in records PROVIDER maintains and associated with the Services (such as Batch Records) but in any event in accordance with applicable Law and time frames provided in patient informed consent forms which have been explicitly notified to PROVIDER. For the purposes of this Section 7.7, "Protected Health Information" or "PHI" has the meaning provided in the U.S. Code of Federal Laws at 45 CFR 160.103 and shall include similar terms as applicable under corresponding foreign laws, such as the EU Data Protection Law. "EU Data Protection Law" means (x), the EU General Data Protection Law ((EU) 2016/679)) of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data ("GDPR"), and any equivalent or replacement law in any country that is a member of the European Union or of the European Economic Area and all and any regulations made under those acts or regulations; (y) the guidelines, recommendations, best practice opinions, directions, decisions, and codes of conduct issued, adopted or approved by the European Commission, the European Data Protection Board, and/or any supervisory authority or data protection authority from time to time in relation to the Directive or the GDPR; and (z) any

judgments of any relevant court of law relating to the processing of personal data, data privacy, and data security.

7.8. Trademarks and Trade Names. CLIENT and PROVIDER hereby acknowledge that neither party has, nor shall either party acquire by reason of this Agreement, any interest or rights of use in any of the other party's trademarks, trade names, designs or logos unless otherwise expressly agreed in writing by the parties. Notwithstanding the foregoing, CLIENT shall have the right to use the PROVIDER'S trademarks, trade names, designs or logos, as may be required by applicable Laws (or as may otherwise be reasonably necessary) in connection with obtaining and maintaining Health Registrations for the Products or in connection with marketing and sale of Product (e.g., listing PROVIDER as the manufacturer of product on the packaging, if applicable).

7.9. Non-Use. Under no circumstances will PROVIDER (or any of its Affiliates) use any CLIENT Manufacturing Know-How (or any other intellectual property rights of CLIENT or any of its Affiliates) or the Confidential Information of CLIENT or any of its Affiliates to manufacture, for itself or for any other person or entity other than for CLIENT and its Affiliates pursuant to this Agreement, any product at any time, or for any other purpose other than for the Manufacture of Product for CLIENT and its Affiliates hereunder, and such obligation not to use CLIENT Manufacturing Know-How, or such intellectual property rights and Confidential Information shall survive the expiration or termination of this Agreement.

ARTICLE 8 - REPRESENTATIONS, WARRANTIES AND COVENANTS.

PROVIDER represents, warrants and covenants to CLIENT as follows in Sections 8.1 through 8.10:

8.1. Standard of Performance. PROVIDER will perform the Services required hereunder in full compliance with the terms of this Agreement (including the relevant Task Order and Quality Agreement), all applicable Batch Records, SOPs, and Laws, and in a competent manner in conformance with the standard of care usually and reasonably expected for the performance of such activities by experienced personnel.

8.2. Laboratory Testing Non-Compliance - Limited Service Warranty. In the event that it is necessary to re-perform any laboratory testing related to a Project originally performed by PROVIDER hereunder due to PROVIDER'S determination that it had failed to comply with Section 8.1, then PROVIDER, shall re-perform such non-complying laboratory testing at its own costs.

8.3. Nonconforming Product - Limited Service Warranty. Product shall:

(a) conform to the applicable Certificate of [***], which includes the Technical Specifications,

(b) have been Manufactured, stored, processed, shipped, disposed of or otherwise handled in accordance with applicable SOPs, Batch Records (including the Master Batch Record), the terms of this Agreement (including the Quality Agreement), cGMPs, and other applicable current Laws,

(c) not be adulterated or misbranded under the FDC Act or other applicable Laws as a result of any act or omission of PROVIDER or any person or entity for which PROVIDER is responsible, and

(d) not be an article which may not, under the provisions of the FDC Act or other applicable Laws, be introduced into interstate commerce as a result of any act or omission of PROVIDER or any person or entity for which PROVIDER is responsible.

If Product fails to comply with the foregoing warranty and such non-conformance is due to PROVIDER'S failure to comply with the terms of this Agreement including the terms in Section 8.1 ("Nonconforming Product"), PROVIDER will at no cost to CLIENT (excluding raw material costs, which shall be the financial responsibility of the CLIENT unless the breach of this warranty was due to the gross negligence or intentional misconduct of PROVIDER or any person or entity for which PROVIDER is responsible), and as soon as commercially reasonable, re-perform the contracted Services. In addition, PROVIDER will, at its sole cost and expense, destroy all Nonconforming Product and promptly provide a certificate of destruction to CLIENT unless otherwise directed by CLIENT. In the event the re-performance of the contracted Services results in Nonconforming Product under the requirements of this Section 8.3, Client agrees to consider in good faith, input from PROVIDER as to whether: (i) PROVIDER should attempt further re-performance of the Services, or (ii) PROVIDER to issue a refund (excluding raw material costs) for the portion of the Non-Conforming Product to CLIENT. In the event of a Nonconforming Product, PROVIDER shall conduct a Quality investigation as outlined in the Quality Agreement. If the result of Quality investigation determines that the Nonconforming Product was at no fault of PROVIDER, the CLIENT shall be responsible for full payment of the Services.

8.4. Debarment Certification (Generic Drug Enforcement Act of 1992). Neither it, nor any of its employees, agents or subcontractors or any other person or entity for which PROVIDER is responsible who will participate in the performance of the Services or in any other work to be performed for or on behalf of CLIENT, have been, are currently, or are the subject of a proceeding that could lead to their or such employees or agents becoming, as applicable, a Debarred Entity, Debarred Individual, Excluded Entity, Excluded Individual, Convicted Entity, or Convicted Individual. PROVIDER further covenants, represents and warrants that if, during the term of this Agreement, it, or any of its employees, agents or subcontractors or any other person or entity for which PROVIDER is responsible participating in the performance of a Project, become or are the subject of a proceeding that could lead that party, employee or agent becoming, as applicable, a Debarred Entity, Debarred Individual, Excluded Entity, Excluded Individual, Convicted Entity or Convicted Individual, then it shall immediately notify CLIENT, and CLIENT shall have the right to immediately terminate this Agreement.

8.5. Training, Licenses and Appraisals. PROVIDER'S applicable personnel have all training, licenses, approvals, certifications, immunizations, equipment and information necessary for safely and properly performing the Services. PROVIDER will ensure that all such training, licenses, approvals, certifications, immunizations, equipment and information are properly maintained throughout the term hereof.

8.6. No Conflicting Obligations. PROVIDER is not nor shall be subject to any conflicting obligation or legal impediment that might preclude or interfere with its performance of its obligations under this Agreement, or that might impair the acceptance of the resulting Deliverable and/or data by the Agency or other regulatory authorities, and that no such obligations will be incurred or permitted in the future without the prior written approval of CLIENT. PROVIDER is duly organized and validly existing under the laws of the country or state of its organization and has full corporate power and authority to enter into this Agreement and to carry out the provisions of this Agreement. PROVIDER is duly authorized to execute and deliver this Agreement and to perform its obligations under this Agreement. The individual executing this Agreement on PROVIDER'S behalf has been duly authorized to do so by all requisite corporate action. This Agreement is a legal and valid obligation binding upon PROVIDER and enforceable in accordance with its terms, subject to applicable bankruptcy, fraudulent transfer, moratorium or other laws affecting the enforcement of creditors' rights and to general principles of equity.

8.7. Accurate Information. Consistent with prevailing industry practices, all data, reports, forms or any other records generated pursuant to a Project by PROVIDER, its agents, employees, subcontractors shall be true and accurate and shall contain no false or misleading information.

8.8. Good Title. CLIENT will have good and marketable title, free and clear of any liability, pledge, lien, restriction, claim, charge, security interest and/or other encumbrance, to all Product and other Deliverables delivered hereunder.

8.9. Permits. PROVIDER has obtained, and will maintain, all Permits necessary for the operation of the Facility and supply of Products and other Deliverables.

8.10. Intellectual Property. To PROVIDER'S best knowledge, PROVIDER owns or has the right to use all intellectual property rights necessary or useful to Manufacture Products as contemplated by this Agreement, and to otherwise carry out its activities hereunder, and such intellectual property rights do not infringe or misappropriate the intellectual property rights of any Third Party and it is not aware of any infringement or misappropriation of its intellectual property rights by any Third Party.

8.11. CLIENT Representations and Warranties. CLIENT represents and warrants that: (a) the execution, delivery and performance of this Agreement does not conflict with, violate or breach any agreement to which CLIENT is a party or CLIENT'S constituent documents; (b) CLIENT is not prohibited or limited by any law or agreement to which it is a party from entering into this Agreement; (c) the performance of any other business or activity engaged in by CLIENT will not interfere in any material respect with CLIENT'S performance under this Agreement; (d) to CLIENT'S knowledge, the CLIENT Materials and CLIENT Technology when used in compliance with this Agreement do not and will not violate any third party's intellectual property rights, and CLIENT has the right to provide such CLIENT Materials and CLIENT Technology to PROVIDER for the purposes of this Agreement; and (e) to CLIENT'S knowledge, the CLIENT Equipment, when provided to PROVIDER, is in good working condition has been properly maintained and stored in good condition and repair, has no known defects or damage, and is fit for the purposes for which it is being provided.

8.12. Failure to Meet Milestone, Remedy. During Process Development and non-cGMP Manufacture, if PROVIDER fails to achieve any milestone and such failure was not the result of either (a) CLIENT'S acts or omissions other than those to enforce its rights under this Agreement, or (b) Force Majeure Events or (c) other factors that are outside of PROVIDER'S reasonable control then PROVIDER will re-perform the relevant activities, at PROVIDER'S expense, in order to attempt to meet the applicable milestone. If after such re-performance PROVIDER is unable again to meet the applicable milestone and such failure was again not the result of any factor that falls within clauses of this Section 8.12, then, subject to Section 10.8, either party may elect to terminate the applicable Task Order upon [***] prior written notice to the other party. Notwithstanding anything to the contrary in this Agreement, as long as PROVIDER has not breached its obligations under this Agreement, including the obligation to exercise commercially reasonable efforts to achieve a Process Development or non-cGMP Manufacture milestone, failure to achieve such milestone, either initially or on a second attempt as provided in this Section, will not be deemed a breach of this Agreement including, but not limited to, any warranty herein.

ARTICLE 9 - INDEMNIFICATION AND INSURANCE

9.1. Indemnification by PROVIDER. PROVIDER shall defend, indemnify, and hold harmless CLIENT, its Affiliates, and its and their respective officers, employees, directors, agents, subcontractors, advisors, agents and consultants, from and against any and all claims, actions, liabilities, losses, demands, damages, fines, penalties, costs and expenses (including reasonable attorneys' fees) (collectively, "Losses") related to or resulting from any claim, action, demand, or proceeding asserted or brought by a third party (a "Third Party Claim") arising out of or in connection with:

(a) [***]

***except that*** PROVIDER shall have no obligation under the forgoing to the extent the Losses or Third Party Claims are due to CLIENT'S negligence or willful misconduct (or that of any of its Representatives or any other person or entity for CLIENT is responsible), or any CLIENT breach of any representation, covenant or warranty, of this Agreement.

9.2. Indemnification by CLIENT. CLIENT shall indemnify, defend and hold harmless PROVIDER, its Affiliates and its or their directors, officers and employees from and against all Losses arising from any Third Party Claim to which PROVIDER is or may become subject to the extent caused by:

(a) [***]

(b) [***]

(c) [***]

(d) [***]

(e) [***]

(f) [***]

(g) [***]

***except that*** CLIENT shall have no obligation under the forgoing to the extent the Losses or Third Party Claims fall under, or are covered by, PROVIDER'S defense and indemnification obligations under Section 9.1 above.

9.3. Indemnification Procedure.

(a) If any Third Party Claim is brought against a party entitled to indemnification under this Section 9 (each, an "Indemnified Party"), such Indemnified Party or Parties shall promptly notify the party obligated to provide indemnification (an "Indemnifying Party") in writing of the institution of such Third Party Claim.

(b) Promptly upon receipt of notice, the Indemnifying Party shall promptly assume the defense of such Third Party Claim including the employment of counsel reasonably satisfactory to such Indemnified Party or Parties, and payment of expenses. An Indemnified Party or Parties shall have the right to employ its or their own counsel in any such case, but the fees and expenses of such counsel shall be at the expense of such Indemnified Party or Parties, unless:

(i) the employment of such counsel shall have been authorized in writing by the Indemnifying Party in connection with the defense of such action; or

(ii) the named parties to such action include both the Indemnified Party or Parties and the Indemnifying Party and such Indemnified Party or Parties shall have reasonably concluded that there may be one or more legal defenses available to it or them or to other Indemnified Parties which are different from, or in addition to, those available to the Indemnifying Party.

In either of the foregoing events in clauses (i) or (ii), such fees and expenses shall be borne by the Indemnifying Party and the Indemnifying Party shall not have the right to direct the defense of such action on behalf of the Indemnified Party or Parties. Notwithstanding anything to the contrary set forth herein, under no circumstances shall the Indemnifying Party be obligated to assume responsibility for the expenses for more than one counsel for all the Indemnified Parties.

(c) Notwithstanding anything contained in this Section 9 to the contrary, the Indemnifying Party shall not be liable for any settlement of any such Third Party Claim effected without its written consent, which consent shall not be unreasonably withheld. The Indemnifying Party shall have the right to settle or compromise any Third Party Claim, or permit a default or consent to the entry of judgment in, or otherwise seek to terminate, any pending or threatened Third Party Claim, in respect of which indemnity may be sought hereunder (whether or not any Indemnified Party is a party thereto), provided such settlement, compromise, consent, or termination includes an unconditional release of each Indemnified Party from all liability in respect of such Third Party Claim. In the event such an unconditional release is not obtainable for each Indemnified Party, then the Indemnifying Party must obtain the prior written consent of any Indemnified Party not so released before the Indemnifying Party may enter into such settlement, compromise, consent or termination.

9.4. Consequential Damages - Limited Liability, Limited Warranty, Limitation on Damages.

(a) EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATIONS OR WARRANTIES OF ANY KIND WHATSOEVER, EITHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY, OR WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE, OR WARRANTY OF NON-INFRINGEMENT, WHETHER ARISING BY LAW, COURSE OF DEALING, COURSE OF PERFORMANCE, USAGE OF TRADE OR OTHERWISE, ALL OF WHICH ARE EXPRESSLY DISCLAIMED.

(b) NOTWITHSTANDING ANYTHING IN THIS AGREEMENT, INCLUDING THE QUALITY AGREEMENT, OR IN ANY TASK ORDER, TO THE CONTRARY, EXCEPT AS SET FORTH BELOW: (I) NEITHER PARTY SHALL BE LIABLE UNDER ANY LEGAL THEORY (WHETHER TORT, CONTRACT OR OTHERWISE) FOR SPECIAL, INCIDENTAL, CONSEQUENTIAL, PUNITIVE OR ANY OTHER INDIRECT DAMAGE OR LOSS (INCLUDING LOST PROFITS) SUSTAINED BY THE OTHER PARTY OR ANY OTHER PERSON OR ENTITY ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE UNDERLYING DELIVERABLE(S), REGARDLESS OF ANY NOTICE OF SUCH DAMAGES; AND (II) UNDER NO CIRCUMSTANCES SHALL PROVIDER'S AGGREGATE LIABILITY FOR ANY AND ALL CLAIMS ARISING OUT OF OR IN CONNECTION WITH A DELIVERABLE UNDER THIS AGREEMENT EXCEED [***] THE AMOUNT ACTUALLY RECEIVED OR TO BE RECEIVED BY PROVIDER FROM CLIENT UNDER THE APPLICABLE TASK ORDER FOR SUCH DELIVERABLE. ALL CLAIMS RELATING TO A SPECIFIC DELIVERABLE MUST BE BROUGHT WITHIN [***] OF DELIVERY TO CLIENT (OR ITS DESIGNEE) OF THE APPLICABLE DELIVERABLE, REGARDLESS OF THEIR NATURE. IN NO EVENT SHALL PROVIDER BE LIABLE FOR ANY LOSS OR DAMAGE TO CLIENT'S IN-PROCESS COMMERCIAL PRODUCTS (NONE OF WHICH SHALL BE MANUFACTURED UNDER THIS AGREEMENT).

(c) ***NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 9 IS INTENDED TO OR SHALL LIMIT OR RESTRICT THE DAM A GES TH A T CLIENT MA Y PURSUE AND RECOVER (I) WITH RESPECT TO A BREACH BY PROVIDER OF ITS OBLIGATIONS UNDER ARTICLE 7, (II) IN CONNECTION WITH***

***PROVIDER'S DEFENSE AND INDEMNIFICATION OBLIGATIONS UNDER SECTION 9.1(b) OR (c), FOR WHICH SUCH PROVIDER'S INDEMNIFICATION LIABILITY FOR A CLAIM SHALL BE LIMITED TO*** [***] ***THE TOTAL AMOUNTS ACTUALLY RECEIVED BY PROVIDER FROM CLIENT UNDER THE APPLICABLE TASK ORDER, OR (III) IN THE CASE OF GROSS NEGLIGENCE, RECKLESSNESS, OR WILLFUL MISCONDUCT.***

9.5. Insurance.

(a) Without limiting its liability under this Agreement (except as may be otherwise expressly provided in this Agreement), during the term of this Agreement and for [***] after the expiration or termination of this Agreement, CLIENT shall obtain and maintain with financially sound carriers commercial general liability and product liability insurance with limits of not less than $[***] per occurrence for general liability and product liability. With respect to all insurance coverage required under this Section 9.5(a), (i) CLIENT shall, promptly upon PROVIDER'S request, furnish PROVIDER with certificates of insurance evidencing such insurance and (ii) all policies shall include provisions for at least [***] prior written notice of cancellation. PROVIDER shall be named as an additional insured under the policies of insurance required by this Section.

(b) Without limiting its liability under this Agreement (except as may be otherwise expressly provided in this Agreement), during the term of this Agreement and for [***] after the expiration or termination of this Agreement, PROVIDER shall obtain and maintain with financially sound carriers commercial general liability and product liability insurance with limits of not less than $[***] per occurrence for general liability and product liability. With respect to all insurance coverage required under this Section, PROVIDER shall, (i) promptly upon CLIENT'S request, furnish CLIENT with certificates of insurance evidencing such insurance (or other similar evidence if self-insured) and (ii) all policies shall include provisions for at least [***] prior written notice of cancellation.

(c) Each party may self-insure all or any portion of the required insurance as long as, together with its Affiliates, its US generally accepted accounting principles (consistently applied) ("GAAP") net worth is greater than $[***] or its annual EBITDA (earnings before interest, taxes, depreciation and amortization) as determined by GAAP is greater than $[***].

ARTICLE 10 - TERM, TERMINATION AND POSTPONEMENT, CANCELLATION, LIQUIDATED DAMAGES

10.1. Term. This Agreement shall begin on the Effective Date and shall remain in full force and effect for [***] or until terminated as provided herein.

10.2. Termination of Agreement. Subject to any and all applicable cancellation, delay, penalty fees and non-refundable deposits or fees, and Sections 10.6 and 10.7, this Agreement may be terminated:

(a) by (i) PROVIDER for convenience and without cause upon [***] prior written notice to the CLIENT and (ii) CLIENT for convenience and without cause upon [***] prior written notice to the PROVIDER;

(b) immediately by CLIENT or PROVIDER upon the material breach of this Agreement by the other party and the failure of such other party to cure such breach within [***] of receipt of the non-breaching party's written notice of such breach, or immediately by either party by written notice to the other party if the other party abandons its operations, becomes insolvent, becomes the subject of voluntary or involuntary bankruptcy, arrangement, composition or other like proceeding, which is not dismissed within [***] of

commencement thereof, makes an assignment for the benefit of its creditors, or consents to the appointment of a trustee, receiver or other fiduciary for all or a substantial part of its assets; or

(c) provided that, unless otherwise provided in such notice and permitted under this Agreement, termination of the Agreement shall not result in termination of any already commenced and uncompleted Task Orders, which shall continue under all terms of this Agreement until completion or termination under Section 10.3 or 10.2(b).

10.3. Termination of Task Orders by CLIENT. Subject to Sections 10.6 and 10.7, CLIENT may terminate without cause any one or more of the Task Orders at any time by giving [***] written notice to PROVIDER. CLIENT'S termination of any Task Order will not result in the termination of this Agreement unless so stated in CLIENT'S written notice of termination to PROVIDER of its decision to terminate or suspend such Task Order. CLIENT'S termination of Task Order, unless due to Provider's breach of this Agreement, has no effect on the non-refundable deposit (if any) which shall be wholly retained by PROVIDER unless the applicable Task Order expressly states otherwise and shall be applied to any applicable amounts payable under Sections 10.3 or 10.6. Further, CLIENT may terminate one or more of the Task Orders at any time upon [***] prior written notice to PROVIDER: (i) following material breach of this Agreement, including material breach of one or more Task Orders, by PROVIDER for the [***], regardless of whether or not PROVIDER has cured such breaches or (ii) PROVIDER is subject to any Agency warning letter or sanction.

If CLIENT terminates a Task Order for convenience under Section 10.3 without terminating this Agreement:

(a) except as provided for below in Section 10.3(d), CLIENT shall pay PROVIDER the following cancellation or termination fee based on the timing of the cancellation or termination relative to the Projects described in the Task Order (as a percentage of the fees for the performance of Services) that is canceled or terminated as follows (Table 10.3).

Table 10.3: Notification of Cancellation or Termination and Percentage of Fees Owed

| Written Notification of Cancellation or Termination to PROVIDER | Percentage of Total Remaining Balance of Fees for applicable services/Batches owed on Task Order |
|---|---|
| [***]or Less or Run in Process | [***] |

(b) subject to Sections 10.4, 10.5, 10.6 and 10.7 below, the parties shall have no further obligations to one another hereunder with respect to such Task Order except for obligations under provisions that survive termination of this Agreement in its entirety;

(c) this Agreement shall remain in full force and effect with respect to all other Task Orders; and

(d) in the event CLIENT terminates a Task Order for convenience under Section 10.3, both parties shall use good faith efforts to reschedule such Project subject to slot availability. PROVIDER shall use commercially reasonable efforts to mitigate the cancellation or termination and fill any available capacity resulting from CLIENT'S cancellation or termination. If PROVIDER is able to fill the capacity, PROVIDER shall waive or reduce CLIENT'S cancellation or termination fees as set forth above to reflect the revenue to be paid by such replacement work. CLIENT shall pay a pro-rated cancellation or termination

fee in the event PROVIDER is able to partially fill the available capacity due to CLIENT'S cancellation or termination.

10.4. Procedures on Termination. Upon termination of this Agreement or a Task Order:

(a) PROVIDER shall fully cooperate with CLIENT requests to provide for an orderly wind down of the Services provided therefor, and, if CLIENT elects to continue any of the Projects in the event of a termination of this Agreement, an orderly transfer of PROVIDER's responsibilities with respect to such Projects to CLIENT or its designee;

(b) PROVIDER shall, as directed by CLIENT:

(i) deliver all Project Records to the location designated by CLIENT; or

(ii) retain all Project Records in accordance with Section 3.3 herein; or

(iii) dispose of all Project Records in accordance with all applicable Laws unless PROVIDER is otherwise required to retain copies of such materials, information, databases and records, accounts, notes, reports or data under applicable law or Laws (in which case, PROVIDER shall retain one copy of all such materials, information, databases and records, accounts, notes, reports and data for the time required by applicable Laws and such items shall continue to be subject to the provisions of Article 7).

For avoidance of doubt, PROVIDER agrees to conduct the activities required hereunder at the time and in the manner requested by CLIENT. All costs of delivering items to CLIENT pursuant to this Section, including shipping costs, or of disposing or retaining the same shall be borne by CLIENT. In no event will PROVIDER dispose of any Project Records without first giving CLIENT [***] prior written notice of its intent to do so and complying with any directions or written requests provided by CLIENT during such notice period.

10.5. Effect of Termination of Task Orders or Agreement.

(a) The termination of any Task Order shall have no effect on the continued existence and enforceability of this Agreement. The termination of this Agreement shall mean that any and all pending Task Orders that have not been executed by the parties shall not go into effect. Except as expressly set forth in this Agreement, termination of this Agreement or a Task Order shall not relieve CLIENT from (i) any and all applicable cancellation, delay, penalty fees and non-refundable deposits or fees, (ii) other damages (including liquidated damages), if any, (iii) any accrued but unpaid obligations for Services properly performed, and (iv) expenses properly incurred by PROVIDER prior to such termination date that are reimbursable by the CLIENT under this Agreement or for reasonable, non-cancelable expenses properly incurred by PROVIDER consistent with the terms of the Task Order and in accordance with this Agreement prior to the date of notice of termination (including any non-cancelable expenses so incurred but payable after the effective date of termination) which would otherwise have been payable by CLIENT under the terms of this Agreement. PROVIDER shall use its commercially reasonable efforts to mitigate and minimize the amount of non-cancelable obligations which could be payable by CLIENT following termination and in no event shall the amount payable by CLIENT in the event of early termination exceed what would have been payable had there not been early termination.

(b) Upon expiration or termination of this Agreement in its entirety or with respect to one or more individual Task Orders, as the case may, PROVIDER shall provide reasonable

assistance and support to CLIENT in connection with any transfer of the Manufacturing process to another facility, including a Third Party facility, and such Services shall be described in an applicable Task Order. CLIENT and PROVIDER shall enter into a Task Order to facilitate such transfer in customary and mutually agreeable form, with PROVIDER providing no more than [***] to support said transfer activities for no more than [***] of time and no more than $[***] (USD). Pursuant to written request from CLIENT to PROVIDER, PROVIDER shall transfer to CLIENT and/or its designee any and all CLIENT intellectual property in PROVIDER'S possession and shall provide to CLIENT and/or its designee PROVIDER intellectual property, so as to permit CLIENT and/or its designee(s) to produce/Manufacture Products with such technical assistance being provided as set forth above and in accordance with a plan provided to PROVIDER by CLIENT.

10.6. Delay Policy; Fees.

In the event of a delay is requested by or caused by CLIENT, and that Client cause is (a) not due to a breach of this Agreement by PROVIDER , (b) outside of Provider's reasonable control, or (c) due to a Force Majeure Event, CLIENT shall pay the amounts set forth below in this Section 10.6 (which, for clarity, shall cover, without limitation, all amounts otherwise due for: CLIENT Materials, use of single sourced materials, or CLIENT-designated product-specific materials, CLIENT shall pay to PROVIDER costs for all non-cancelable work and unearned payments for the duration of the term for the delay, including expired materials, labor and suite fee charges that cannot be reallocated, all work in progress including third party services that through the term of the delay).

PROVIDER and CLIENT will work in good faith to limit the costs associated with the delay. PROVIDER maintains the rights to stop all work in progress and allocate resources to limit additional costs incurred. Such delays may be withdrawn by written notice to PROVIDER, specifying a mutually agreed upon date for return to service by both parties.

The below Table 10.6 - Notification of Delays and Percentage of Fees Owed, are the obligation of CLIENT. The policy and fees are effective as of Project initiation date(s) described in the mutually- agreed to in the signed Task Order. Percentages are applied to the total cost of fees for the individual Project that is delayed. In the event of a delay, both parties shall use good faith efforts to reschedule such Project.

Table 10.6 - Notification of Delay Fees Owed

| Written Notification of Delay<br>Requested or Caused by CLIENT to PROVIDER | Delays<br>Percentage of Total Remaining Balance of Fees for applicable services/Batches owed on Task Order |
|---|---|
| [***] | [***] |

1. Any request by the CLIENT to hold materials in-process at a specific stage within the Manufacturing process, which is before a billable event, will result in a pro-rata invoice from PROVIDER to CLIENT.

2. In the event of a CLIENT-caused or requested delay, both parties shall use good faith efforts to reschedule such Project subject to slot availability. PROVIDER shall use commercially reasonable efforts to mitigate the delay and fill any available capacity resulting from CLIENT'S delay. If PROVIDER is able to fill the capacity, PROVIDER shall waive or reduce CLIENT'S Delay Fees as set forth above to reflect the revenue to be paid by such replacement work. CLIENT

shall pay a pro-rated Delay Fee in the event PROVIDER is able to partially fill the available capacity due to CLIENT'S delay.

3. In the event of a PROVIDER-caused delay, PROVIDER shall use good faith efforts to reschedule such Project to the next available slot subject to slot availability within the Facility.

10.7. Liquidated Damages. CLIENT acknowledges that the actual damages likely to result from breach of Sections 10.3 and 10.6 are difficult to estimate on the date of this Agreement and will likely cause PROVIDER to incur economic damages and other losses of types and amounts that would be difficult for PROVIDER to prove. The parties intend that CLIENT'S forfeit of the non-refundable deposit and/or payment of any delay, suspension, cancellation or termination fee, whichever the case may be individually or collectively, is fair and reasonable compensation and payment as liquidated damages and would serve to compensate PROVIDER for any delay, suspension, cancellation or termination by CLIENT under Sections 10.3 or 10.6, and they do not intend for it to serve as punishment for any such delay, suspension, cancellation or termination by CLIENT.

10.8. Termination for Technical Problems. If during the performance of Services under a Task Order in accordance with the terms of this Agreement, either party identifies in good faith an unforeseeable technical problem not caused by the act or omission of the PROVIDER (or any person or entity for which the PROVIDER is responsible) that prevents PROVIDER from achieving a milestone or the Specifications identified in that Task Order, then the following procedures will apply:

(a) PROVIDER may request reasonable further technical assistance from CLIENT and CLIENT will use commercially reasonable efforts to provide such technical assistance.

(b) The parties will discuss and consult with each other regarding the technical problem, and will use commercially reasonable efforts to resolve the problem.

(c) The additional cost of resolving the problem, to the extent approved by the Client in writing, shall be described in a relevant Task Order and will be borne by CLIENT except to the extent that the problem has occurred through fault of PROVIDER (or its employees, subcontractors, or any other person or entity for which it is responsible).

If the parties are unable to resolve the problem to the satisfaction of both parties within [***] from identification thereof, unless the parties are progressing to a mutually agreeable resolution of the problem, then either party may terminate the affected Task Order upon [***] prior written notice to the other party; provided that Client may not terminate under this Section if the problem is due to Client's acts or omissions.

10.9. Return of CLIENT Supplied Materials and other Information. Upon termination or expiration of this Agreement (or upon termination of a given Task Order, as applicable) for any reason, or at any time during the term of this Agreement, in each case upon CLIENT'S written request and so long as CLIENT has paid all undisputed outstanding amounts due to PROVIDER at that time, PROVIDER shall promptly deliver to CLIENT: (a) all CLIENT Equipment, unused Drug Substance and/or Drug Product and other CLIENT Materials in PROVIDER'S (or any of its Affiliates' or its or their respective subcontractors') possession or control; (b) all documentation and all copies thereof in whatever form or medium in PROVIDER'S (or any of its Affiliates' or its or their respective subcontractors') possession or control relating to Technical Specifications, CMCs, or CLIENT Manufacturing Know-How; and (c) all other Confidential Information of CLIENT and any and all other documents and materials (and all copies thereof) in PROVIDER'S (or any of its Affiliates' or its or their respective subcontractors') possession or control relating to Product and/or containing any Confidential Information of CLIENT other than any CLIENT Confidential Information which the PROVIDER must retain for such period of time as required by applicable Law; provided, however, that the provisions

of this Agreement relating to such CLIENT Confidential Information shall apply to such Confidential Information for so long as it is so retained notwithstanding the expiration or termination of this Agreement. Notwithstanding the foregoing, to the extent that only a given Task Order is terminated, then the foregoing provisions shall only apply to the terminated Task Order(s) and the Product(s) thereunder.

ARTICLE 11 - MISCELLANEOUS

11.1. Subcontracting.

(a) If consented to in writing by CLIENT or the applicable CLIENT Affiliate, an Affiliate of PROVIDER may directly Manufacture a given Product hereunder for CLIENT (or its Affiliate, as applicable) by such Affiliate entering into a Task Order for such Product. Each such Affiliate of PROVIDER that enters into a Task Order shall be bound by the terms of this Agreement with respect to the Product which is the subject of the applicable Task Order executed by such Affiliate and shall have all of the rights and obligations of PROVIDER under this Agreement with respect to such Product. The execution of a Task Order hereunder by such Affiliate shall be evidence of its consent to be so bound. Notwithstanding the foregoing, PROVIDER shall remain fully responsible and liable for all obligations hereunder and assumes full vicarious liability for any Affiliate performing under any given Task Order.

(b) PROVIDER may not subcontract the performance of any of the Services to non-Affiliate Third Parties without CLIENT'S prior written consent. PROVIDER shall at all times remain primarily liable for the full and proper performance of all of its obligations under this Agreement and shall be solely responsible for the oversight of all permitted subcontractors. If the Services require PROVIDER to pay any permitted Third Parties and that applicable Task Order specifically provides that CLIENT will provide the funding for such Third Parties, PROVIDER agrees that it shall disburse promptly funds received from CLIENT to the appropriate third parties.

(c) Notwithstanding Section 11.1(b) above, PROVIDER shall be responsible for ensuring that its contracts with approved subcontractors are consistent with the terms of this Agreement and the respective Task Order and shall permit CLIENT to audit such subcontractor as provided herein. CLIENT'S consent to the use of any subcontractor shall not be deemed to relieve PROVIDER of any of its obligations hereunder, and PROVIDER shall at all times remain primarily liable for performance of all such obligations.

11.2. Non-Solicitation. During the period during which this Agreement is in effect, and for [***] thereafter, neither party shall recruit or solicit, directly or through a third party, any employee of the other party materially involved in the performance of this Agreement ("Covered Employees") without the prior written consent of the other party. The foregoing shall not prohibit general solicitations, such as ads placed in newspapers or trade journals, use of internet job boards or social media sites, engagement of professional recruiters or participation in job fairs, not specifically directed at the Covered Employees.

11.3. Publicity. Except to comply with applicable Laws, neither party hereto shall use the name of the other party or its employees or trademarks in any press release, publicity, advertising, or other disclosure without prior written consent of the other party hereto.

11.4. Independent Contractors. For purposes of this Agreement, the parties agree that they are and will be acting solely as independent contractors and nothing contained in this Agreement is intended or shall be construed to place them in the relationship of partners, principal and agent,

employer/employee or joint ventures, nor to give either party the authority to legally bind the other party, and neither party shall hold itself out as having such authority.

11.5. Amendments. This Agreement may not be amended or modified in any manner except by an instrument in writing signed by both authorized representatives of the parties hereto.

11.6. Assignment. Neither party may assign or otherwise transfer any of its rights or obligations under this Agreement without the prior written consent of the other party, which will not be unreasonably withheld, except that a party may assign, in whole or in part, without such consent any of its rights or obligations under this Agreement (i) to any Affiliate of such party, provided that any such assignment to an Affiliate shall not relieve PROVIDER as the primary obligor hereunder, or (ii) to a successor in interest in connection with the merger, consolidation, or sale of the stock or substantially all of the assets of the party's business responsible for the performance of this Agreement, provided that neither party shall have the right to assign or transfer this Agreement to a competitor of the other party. Further, without PROVIDER'S consent, CLIENT may assign this Agreement, on a Product-by-Product basis, in connection with any divestiture or out-licensing of a Product. Any other attempted assignment in violation of this Section 11.6 shall be void. This Agreement shall inure to the benefit of and be binding on CLIENT, PROVIDER and their respective permitted successors and assigns.

11.7. Entire Agreement. This Agreement (which includes the Exhibits hereto, the Quality Agreement, and executed Task Orders hereto) constitutes the entire agreement and understanding of the parties with respect to the subject matter hereof, and it supersedes all prior oral and written agreements, commitments or understandings with respect to the matters provided for herein, including (a) any prior confidentiality agreement, memorandum of understanding, letter of intent or letter of agreement, except that any Confidential Information related in any way to this Agreement disclosed under any prior confidentiality agreement, etc. shall be deemed disclosed under this Agreement and subject to the terms herein, and (b) the MGA, provided that the MGA shall be deemed to be a Task Order under and subject to the terms of this Master Production Services Agreement. In the event of any conflict between the other terms of this Agreement and any Task Order or Schedule or Exhibit hereto, the other terms of this Agreement shall govern unless otherwise specifically set forth in a Task Order; provided that in the event of any conflict between the terms of this Agreement and the MGA, the terms of this Agreement shall govern and control. In accordance with Section 2.1a, in the event of any discrepancy or inconsistency between the tasks listed in such Quality Agreement and the other terms of this Agreement, the terms of Quality Agreement will govern with respect to quality matters and other similar matters, and the other terms of this Agreement shall govern with respect to all other matters.

11.8. Governing Law.

This Agreement, the rights and obligations of the parties hereto, and any claims or disputes relating thereto, shall be governed by and interpreted in accordance with the substantive laws of the Commonwealth of Massachusetts, USA, excluding any choice of law rules that would otherwise apply the law of any other jurisdiction. Any and all disputes arising under this Agreement shall be exclusively adjudicated in a state or Federal court of competent jurisdiction located in Boston, Massachusetts, USA (and the appropriate appellate courts therefrom), and each party irrevocably submits to the exclusive jurisdiction of such courts in any suit, action or proceeding and irrevocably waives any objection based on inconvenient forum or lack of personal jurisdiction.

11.9. Notices. All notices, demands, requests, or other communications which may be or are required to be given, served, or sent by any party to any other party pursuant to this Agreement (collectively, "Notices") shall be in writing and, except where this Agreement elsewhere expressly permits e-mail notices, shall be mailed by first-class, registered or certified mail, return receipt requested, postage

prepaid, hand-delivered (including delivery by courier), or sent by recognized express courier (such as FedEx, UPS, DHL) as follows:

If to CLIENT

Candel Therapeutics, Inc.
117 Kendrick St., Suite 450
Needham, MA 02494
Attention: Chief Development and Technical Officer

If to PROVIDER

SAFC Carlsbad, Inc.
6211 El Camino Real
Carlsbad, CA 92009
Attention: Site Director

With a copy to:

EMD Millipore Corporation
400 Summit Drive
Burlington, MA 01830 USA
Attn: General Counsel

Either party may designate by notice in writing a new address or contact person by notice given in accordance with this Section 11.9. Each Notice shall be deemed received at such time as it is delivered to the addressee (with the delivery receipt being deemed conclusive (but not exclusive) evidence of such delivery) or at such time as delivery is refused by the addressee upon presentation.

11.10. Severability. If any provision of this Agreement is held unenforceable by a court or tribunal of competent jurisdiction because it is invalid or conflicts with any law of any relevant jurisdiction, the validity of the remaining provisions shall not be affected. The parties shall negotiate a substitute provision that, to the greatest extent possible, accomplishes the original business purpose.

11.11. Survival. Neither expiration nor termination of this Agreement shall terminate those obligations and rights of the parties pursuant to this Agreement which by their nature or terms are intended to survive and such provisions shall survive the expiration or termination of this Agreement. Without limiting the generality of the foregoing, the following provisions of this Agreement shall survive any expiration or termination hereof: Articles 3, 5, 7, 8, 9, and 11, Sections 2.1, 2.2, 2.3, 2.7, 4.1, 4.4, 4.5, 4.6, 10.3, 10.4, 10.5, 10.6, and 10.8, and all definitions herein required to interpret the foregoing.

11.12. Waiver. Neither the waiver by a party hereto of a breach of or a default under any of the provisions of this Agreement, nor the failure of a party, on one or more occasions, to enforce any of the provisions of this Agreement or to exercise any right or privilege hereunder shall thereafter be construed as a waiver of any subsequent breach or default of a similar nature, or as a waiver of any of such provisions, rights or privileges hereunder. No waiver by a party hereto of, or consent by a party hereto to, a variation from any provision of this Agreement shall be effective unless made in a written instrument duly executed on behalf of such party.

11.13. Force Majeure. Neither party will be in default of any obligation under this Agreement (other than obligations to pay money unless transmission of funds is delayed or prevented) to the extent

performance is prevented or delayed by a Force Majeure Event. A "Force Majeure Event" shall include any occurrence beyond the reasonable control of a party that is not the results of its fault or negligence or failure to have put reasonable contingency plans in place, including: act of nature (e.g., flood, earthquake or storm); war or terrorism; civil commotion or riot; epidemic or pandemic (e.g., COVID-19); destruction of facilities or materials; biological contamination in a facility; fire or explosion; labor disturbance or strike; laws, regulations, directives or orders of any government, regulatory or judicial authority; embargo, shortage of raw materials or labor; equipment failure; or failure of public utilities or common carriers. The party declaring a Force Majeure Event will promptly notify the other party in writing, explaining the nature thereof, and will also notify the other party of the cessation of any such event. A party declaring a Force Majeure Event will use commercially reasonable efforts to remedy, remove, or mitigate such event and the effects thereof. Upon cessation of the Force Majeure Event, performance of any suspended obligation or duty will promptly recommence. The party not claiming a Force Majeure event shall have the right to terminate this Agreement with written notice effective upon receipt if the Force Majeure event continues to prevent performance by the other party for a period of more than [***]. Notwithstanding the foregoing, in no event shall a Force Majeure event excuse a party from its obligations under Section 9.1 or Section 9.2, as applicable, or excuse PROVIDER from its obligations under Section 4.8.

11.14. Headings. The headings of this Agreement are for ease of reference only and shall not limit or otherwise affect the meaning of the terms and conditions of this Agreement.

11.15. Compliance with Anti-Corruption Laws. In performing the Services for CLIENT, PROVIDER and its employees and agents (i) shall not offer to make, make, promise, authorize or accept any payment or giving anything of value, including but not limited to bribes, either directly or indirectly to any public official, regulatory authority or anyone else for the purpose of influencing, inducing or rewarding any act, omission or decision in order to secure an improper advantage, or obtain or retain business and (ii) shall comply with all applicable anti-corruption and anti-bribery laws and regulations. PROVIDER and its employees and agents shall not make any payment or provide any gift to a third party in connection with PROVIDER's performance of this Agreement except as may be expressly permitted in this Agreement or a Task Order without first identifying the intended third-party recipient to CLIENT and obtaining CLIENT'S prior written approval. PROVIDER shall notify CLIENT immediately upon becoming aware of any breach of PROVIDER'S obligations under this Section. PROVIDER shall require each employee and agent of PROVIDER who will perform Services pursuant to the Agreement to participate in any anti-corruption training reasonably required by CLIENT.

11.16. Equal Opportunity and Compliance with Employment Laws. If applicable to PROVIDER'S Services hereunder, PROVIDER warrants that in providing the goods and/or Services specified herein, PROVIDER will comply with the following laws, executive order, and the regulations promulgated thereunder, as the same may be amended, when applicable: (a) the Vietnam Era Veterans Readjustment Assistance Act of 1974, (b) Executive Order 11246, and (c) the Rehabilitation Act of 1973. Any clause required to be set forth in a document of this type by such laws, administrative regulations or executive orders shall be deemed to be incorporated herein by this reference. PROVIDER shall not discriminate against any employee or applicant for employment because of race, color, religion, sex, national origin, disability, or covered veteran status.

11.17. Counterparts. This Agreement, including any Task Order and the Quality Agreement, may be executed (including by use of industry standard signature software, such as DocuSign®) in one or more counterparts by authorized signatories of each party, each of which counterpart when executed and delivered by facsimile, electronic transmission (such as email of a .pdf), mail or courier service will be an original and all of which shall constitute one and the same Agreement.

11.18. Subject to its compliance with its obligations hereunder, including Section 2.6(b) and Article 7 of this Agreement, nothing in this Agreement shall be construed as restricting PROVIDER'S right to perform similar or same projects for any third party as the projects contemplated by this Agreement.

11.19. Interpretation. In this Agreement, unless otherwise specified: (a) "includes" and "including" and words of similar import shall mean includes and including without limitation; (b) words denoting any gender shall include all genders; (c) words denoting the singular shall include the plural and vice versa; (d) the Exhibit, Schedule and other attachments form part of the operative provision of this Agreement and references to this Agreement shall, unless the context otherwise requires, include references to the Exhibit, Schedule and attachments; (e) references to "Articles", "Sections" and "subsections" in this Agreement shall be to Articles, Sections and subsections respectively, of this Agreement unless otherwise specifically provided; and (f) references to any Articles or Sections include Sections and subsections that are part of the referenced Article or Section (e.g., a section numbered "Section 2.2(a)" would be part of "Section 2.2", and references to "ARTICLE 2" or "Section 2.2" would refer to material contained in the subsection described as "Section 2.2(a)").

Signature Page Follows

IN WITNESS WHEREOF, the parties hereto have duly executed this Agreement, or have caused this Agreement to be duly executed on their behalf, to be binding and effective as of the Effective Date.

**CANDEL THERAPEUTICS, INC.**

By: /s/ Seshu Tyagarajan
Name: Seshu Tyagarajan
Title: Chief Technical and Development Officer
Date: Nov 10, 2022

**SAFC CARLSBAD, INC.**

By: /s/ Nina Bauer
Name: Nina Bauer
Title: Global Head of Commercial BioVV Millipore CTDMO Services
Date: 11/18/2022

## SCHEDULES AND EXHIBITS

Exhibit A Form of Task Order

Exhibit A

Form of Task Order

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**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the registration statements (No. 333-258279 and No. 333-263961) on Form S-8 and (No. 333-266605) on Form S-3 of our report dated March 30, 2023, with respect to the consolidated financial statements of Candel Therapeutics, Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 30, 2023

**Exhibit 31.1**

**CERTIFICATION 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**

I, Paul Peter Tak, certify that:

1. I have reviewed this Form 10-K of Candel Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual

report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2023 By: /s/ Paul Peter Tak

**Paul Peter Tak**
**President and Chief Executive Officer**
***(principal executive officer)***

**Exhibit 31.2**

**CERTIFICATION 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**

I, Jason A. Amello, certify that:

1. I have reviewed this Form 10-K of Candel Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual

report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2023

By: /s/ Jason A. Amello

**Jason A. Amello**
**Chief Financial Officer**
***(principal financial officer and principal accounting officer)***

**Exhibit 32.1**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the filing with the Securities and Exchange Commission of the Annual Report of Candel Therapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2022 (the "Report"), the undersigned President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 30, 2023 By: /s/ Paul Peter Tak

**Paul Peter Tak**
**President and Chief Executive Officer**
***(principal executive officer)***

In connection with the filing with the Securities and Exchange Commission of the Annual Report of Candel Therapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2022 (the "Report"), the undersigned Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 30, 2023 By: /s/ Jason A. Amello

**Jason A. Amello**
**Chief Financial Officer**
***(principal financial officer and principal accounting officer)***